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Pharmacology for Nurses

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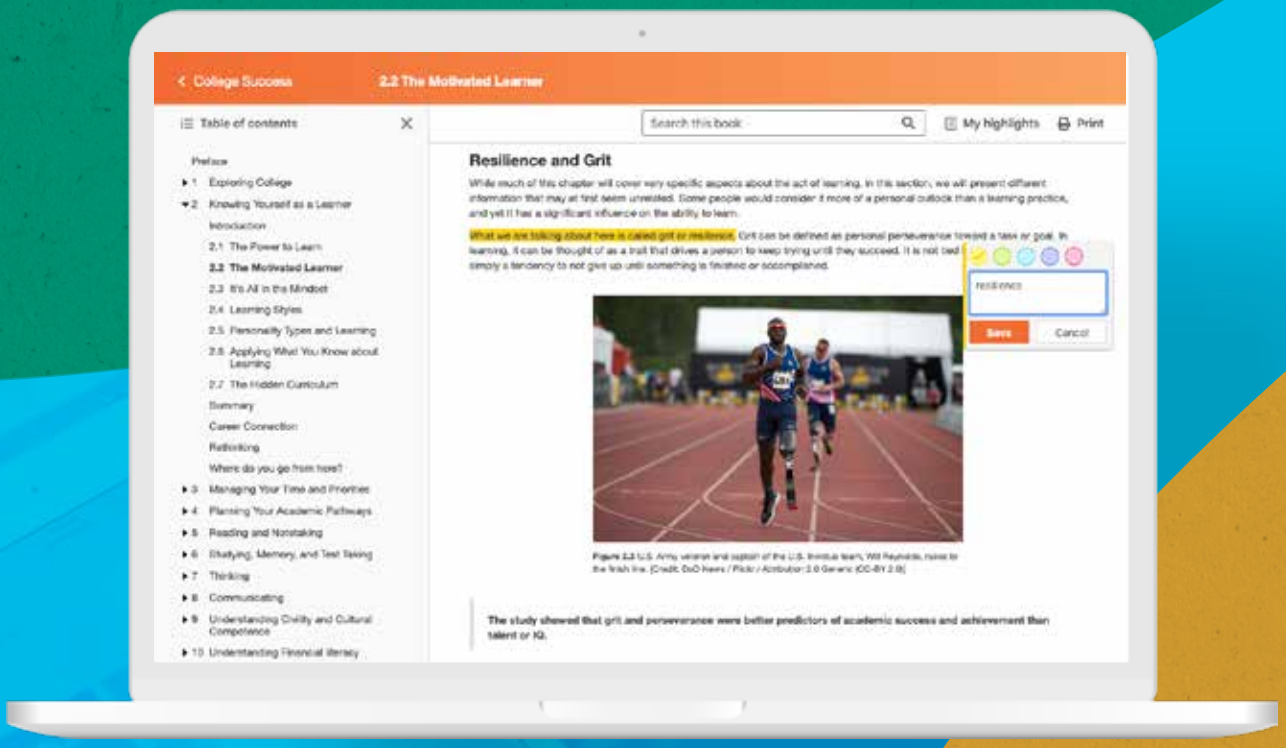

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PREFACE

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About *Pharmacology for Nurses*

Summary

Pharmacology for Nurses aims to provide a fundamental understanding of the therapeutic use of drugs so the nurse can provide safe and effective care to the client. It is important for nursing students to comprehend not only the mechanisms by which drugs impact the human body, but also how the individual's physiological factors influence drug responses. Along with a discussion of each body system, the text also reviews the pathophysiology of various disease processes and medications used in treatment. The textbook is intended for nursing students in an introductory program. *Pharmacology for Nurses* helps students prepare for the licensing exam by offering applicable, real-life content in short, manageable sections; it focuses on common client conditions that nurses will encounter throughout their career and embraces a skills orientation (what does a nurse *do*). Most importantly, *Pharmacology for Nurses* will give students the confidence to safely administer medications to clients as well as

provide medication education to clients and their caregivers.

Pharmacology is often considered one of the more challenging courses in nursing school; however, this book presents the information in a holistic manner that ties the disease process to its pharmacological treatment. This approach will assist students in connecting the pathophysiology of the disease process to the nursing care of the client. Being an effective caregiver requires the nurse to have a solid understanding of the disease process, allowing for the proper assessment and treatment of the client. Due to the number of drugs that are used in clinical practice, one drug is used for each class of medication as a representative drug prototype to help facilitate student learning.

Pedagogical Foundation

Organizational Framework

The table of contents presents 40 chapter topics organized into 11 units. The first unit, consisting of 3 chapters, provides a broad overview of pharmacology, with the following 10 units focused on specific body systems. In each unit, after a review of the body system anatomy, the following chapters discuss pathological conditions and how they are managed and treated with medications.

One of the primary reasons for nurses to learn about pharmacology is to provide safe, effective care of the client; however, it is also important for nurses to be able to educate the client and family about the drugs that have been prescribed. Each chapter has integrated nursing implications and client teaching as features of each class of drugs.

Although the chapters in *Pharmacology for Nurses* are written to be mostly independent, they do generally build on the understanding gained in the previous chapters, including occasional cross-references, particularly within a body system unit. (Please bear this in mind when considering alternate sequence coverage.) Instructors may pair the chapters from this pharmacology textbook with similar body system topics in a disease course.

A working knowledge of basic microbiology, chemistry, and anatomy and physiology will be helpful to students reading this book. To develop sound clinical judgement, students will also need an understanding of the nursing process to link the disease process to the recommended pharmacological treatment.

- **Unit 1** (Chapters 1–3) introduces an overview of pharmacology, drug administration, and quality and safety. Unit 1 also emphasizes the crucial role of ethics in medication administration with a focus on safety, informed consent, and the prevention of medication errors. These ethical considerations are vital in today's health care context, especially given the current legal implications and potential consequences of drug administration errors.
- **Unit 2** (Chapters 4–5) discusses homeostasis within the body and the importance of fluids, electrolytes, vitamins, and minerals in the maintenance of homeostasis. Unit 2 also covers alternative/complementary therapies.
- **Unit 3** (Chapters 6–8) discusses inflammatory response within the body. Unit 3 includes coverage of drugs to treat certain alterations within the immune system, such as infections, cancer, HIV and AIDS, and organ transplants.
- **Unit 4** (Chapters 9–15) discusses the nervous system and provides comprehensive coverage of medications for pain management, substance abuse, and psychotropics for mental health (including anxiety, depression, insomnia, mood stabilization, and psychosis).
- **Units 5–11** (Chapters 16–40) cover medications for system disorders for the cardiovascular, respiratory, endocrine, digestive, renal and urinary, reproductive, sensory, and dermatologic systems. This section of the book also features the topics of weight management, treatment of transgender and nonbinary individuals, and sexually transmitted infections.

Pharmacology Features

To further enhance learning, key in-chapter, medication-related features of *Pharmacology for Nurses* may include:

- **Drug Emphasis Tables:** These tables list common medications in a drug class with typical administration routes and adult dosing. When relevant, pediatric dosing is listed (as an exception). Both generic and brand names of medications are provided, when applicable, to facilitate nurse communication with clients.
- **Drug Prototype Tables:** These tables feature a single representative medication from the preceding drug emphasis table, listing drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications. (When there is only one relevant drug in a class,

only a drug prototype table is provided.)
- **FDA Black Box Warnings:** These feature boxes summarize the boxed warning (https://openstax.org/r/ncbinlm) required by the U.S. Food and Drug Administration (FDA) for medications with serious, permanent, or fatal side effects.
- **Safety Alerts:** These feature boxes summarize additional safety considerations in drug administration and client care, supporting Quality and Safety Education for Nurses (QSEN) (https://openstax.org/r/qsenorgcoa) standards.

Nursing Features

Key in-chapter nursing-related features of *Pharmacology for Nurses*, depending on chapter content, may include:

- **Nursing Implications Sections:** These sections, found throughout the book, emphasize client care considerations, such as which vital signs, medication interactions, and adverse effects to monitor.
- **Client Education Boxes:** These feature boxes list points the nurse should emphasize in client education, such as foods and medications to avoid, symptoms to report, and when to notify the health care provider.
- **Clinical Tips:** These brief feature boxes are practical tips that an experienced nurse might share with a less experienced colleague—for example, the necessity of monitoring a client's blood pressure to evaluate the effectiveness and safety of a drug or assisting clients in making lifestyle adjustments to enhance their blood pressure.
- **Special Considerations Boxes:** These feature boxes highlight differing drug administration and client teaching considerations related to certain client categories, including age/life stage, race/ethnicity/culture, or sex/gender. This feature may serve as an in-class discussion prompt.
- **Case Studies:** These feature boxes present a hypothetical client scenario, listing the client's medical history, current medications, vital signs, and physical examination results. Each scenario is followed by two multiple-choice questions for students to apply their knowledge of evidence-based client care. Some case studies unfold in several parts throughout the chapter, with new information presented on the same client. Case studies can be used as an in-class discussion prompt. The question answers, with explanations, are included in the Answer Key for students at the end of the book.
- **Link to Learning:** These feature boxes provide online resources, videos, and podcasts that are pertinent to students' deeper exploration of the topics. The resources improve nursing students' understanding of how to educate clients about pertinent diseases and medications.
- **Trending Today:** These feature boxes present general health care trends and news from a variety of sources. Boxes may contain online resources and videos. This feature may serve as an in-class discussion prompt.
- **Off-Label Uses:** In some instances, if an "off-label (https://openstax.org/r/fdagovpatie)" use (using an FDA-approved drug for an unapproved indication) is common for a certain medication (such as the prescription of beta blockers for anxiety), the text may mention this so nurses can be aware of the practice.

Pedagogical Features

To support student learning, *Pharmacology for Nurses* includes these standard elements:

- **Learning Outcomes:** Every chapter section begins with a set of clear and concise student learning outcomes. These outcomes are designed to help the instructor decide what content to include or assign and can guide students on what they can expect to learn and be assessed on.
- **Review Questions:** This end-of-chapter feature presents at least 10 multiple-choice questions for students to apply their learned knowledge and integrate the chapter (and unit) concepts. The questions focus on client scenarios, body system and pharmacological concept review, and medication dosing calculations, as relevant to the chapter material. The question answers, with explanations, are included in the Answer Key for students at the end of the book.
- **Chapter Summary:** Chapter summaries assist both students and instructors by outlining the primary subtopics addressed within the chapter.
- **Key Terms:** Key terms are presented in bold text and are followed by an explanation in context. Definitions of key terms are also listed in the end-of-chapter glossary.
- **References:** Key drug information is derived from the manufacturer's FDA-approved labeling via DailyMed (https://openstax.org/r/dailymednl), national guidelines, and peer-reviewed literature when possible. References are listed at the end of the book, organized by chapter.

- **Appendices:** Provided at the end of the book, the appendices include the international system of units, common abbreviations and lab values, and drug conversion tables.
- **Index:** Provided at the end of the book, the index indicates the medications and key topics covered in the book.

About the Authors

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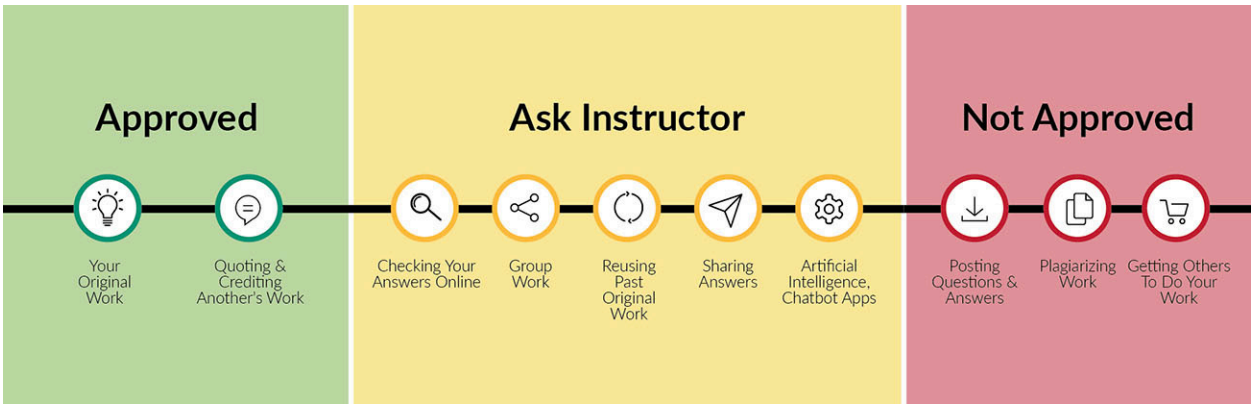

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CHAPTER 1
Introduction to Pharmacology

FIGURE 1.1 Pharmacology is the study of the biological effects of drugs on the body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION This book aims to provide a fundamental understanding of the pharmacological use of drugs that the nurse needs to provide safe and effective care to the client. It is vital to comprehend not only the mechanisms by which drugs impact the human body but also how a client's physiological factors influence drug responses. Along with a discussion of each body system, this text will also review the pathophysiology of various disease processes and medications used in treatment. The field of medicine is constantly changing, and the nurse must stay vigilant about keeping up to date with new drugs and research in disease process. For the nurse, education is a lifelong process.

1.1 Pharmacology, Interdisciplinary Teams, and Nursing Practice

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 1.1.1 Define pharmacology.
- 1.1.2 Identify key events in the history of pharmacology.
- 1.1.3 Discuss the interdisciplinary nature of pharmacology and client care.
- 1.1.4 Explain the importance of pharmacology in nursing practice.

History of Pharmacology

The word **pharmacology** (from two Greek words, *pharmakon*, which means "**drug**" or "medicine," and *logos*, which

means “study”) essentially means the study of medicine; it could also be described as the study of the biological effects of chemicals on the body. The history of pharmacology dates back thousands of years, most likely beginning with the use of medicinal plants and herbs to relieve symptoms of various diseases. Herbal medications have been used in medicine in most civilizations around the globe dating back to ancient times. One generation passed its knowledge to the next through oral tradition. Individuals might not know how a treatment worked, but they were able to observe its effects.

The word *drug* may originate from an old Dutch word, *droog*, which means dry, or an old French term, *drogue*. This may have referred to “dry barrels,” the method for preserving medicinal plants as dry matter or any substance, such as animal products or inorganic materials, used in the composition of medicines. The words *drug* and *medication* are used interchangeably throughout this text.

More than 2,000 years ago in China, Greece, and Egypt, poultices composed of moldy bread were used to treat open wounds. (Was it possible that this had antimicrobial effects?) This treatment was documented in the *Ebers papyrus* (see Figure 1.2), one of the world’s oldest preserved medical documents, in 1550 BCE. Medicinal soils were used at that time as well. An Anglo-Saxon recipe has been found that dates back 1,000 years ago, and it was recently discovered that it is helpful in the treatment of methicillin-resistant *Staphylococcus aureus* (Hutchings et al., 2019).

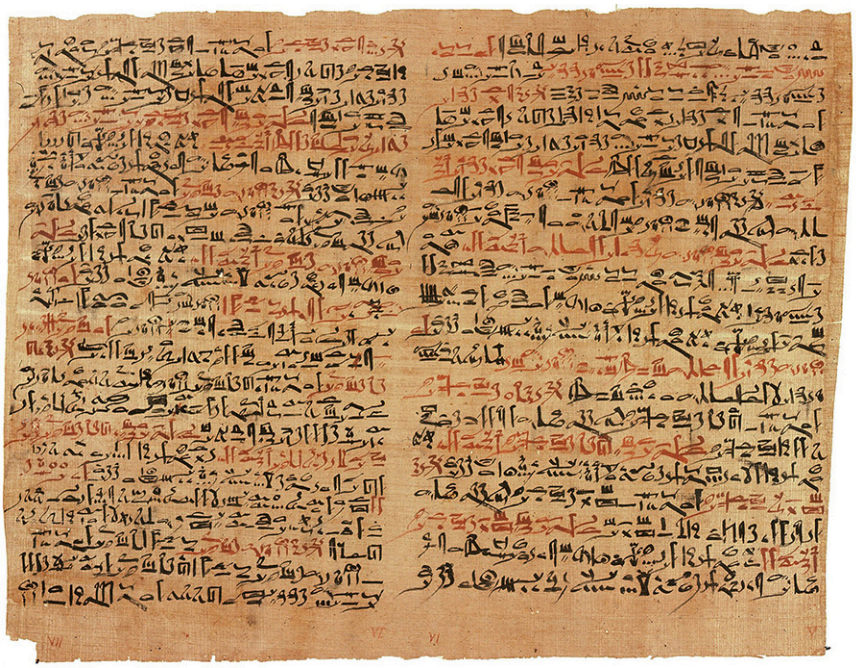


FIGURE 1.2 The Ebers Papyrus is considered one of the oldest preserved medical documents. (credit: “Edwin Smith Papyrus v2” by Jeff Dahl/Wikimedia Commons, Public Domain)

It is true that although many treatments or remedies were simply ineffective, others unfortunately were poisonous. However, some treatments did contain substances that worked. Opium, from the poppy plant, has been used for centuries to relieve pain and for sedation by the Sumerians and the Greeks. However, the first authentic use was recorded by the Greek philosopher Theophrastus in the 3rd century BCE (Stefano et al., 2017).

The *London Pharmacopoeia*, first published in 1618, contained over 1,000 simple drugs and over 900 preparations and compounds. Progress in the use of pharmacological treatments continued to develop worldwide at differing rates, but in the late 1700s, several advances in Europe were made that remain significant today. William Withering in England developed digitalis, a derivative from the foxglove plant, which was and still is used in treating heart disease and rhythm disorders. Foxglove had been used for centuries in folk medicine, but Withering was able to use small amounts of the foxglove leaves for the treatment of dropsy (now known as heart failure). Another advancement occurred in 1796 when Edward Jenner developed the first vaccine against smallpox. His work established that infectious diseases could be controlled with the deliberate use of vaccination.

The era of modern pharmacology began approximately 200 years ago. Even in the early 1800s, chemists could isolate various chemicals from substances and mixtures. In 1804 or 1805, Fredrich Serturner isolated morphine

from opium, which is still used for treating severe pain (Kumar, 2022). Once scientists could isolate the drugs from plants and other natural resources, they could better study their actions on the body. Most often, these experiments were conducted on animals, but occasionally the chemists would test the drug on themselves or on friends and family, sometimes with disastrous results. The first school of pharmacy was established in 1847 in the country of Estonia. The oldest pharmacology journal, *Naunyn-Schmeideberg's Archives of Pharmacology*, was first published in 1873 and is still being published today (Hattori & Seifert, 2023).

Scientists in the 1890s developed aspirin from the bark of the willow tree, using it to treat fevers and mild discomfort. The link between diabetes mellitus and the pancreas was established in 1889 through the work of Joseph von Mering and Oskar Minkowski. Approximately 30 years later, in 1921, Frederick Banting and Charles Best formulated the first insulin preparation (Karamanou et al., 2016; Lee & Yoon, 2021). Paul Ehrlich introduced the first treatment for syphilis in 1909 by isolating a chemical compound that could be used against a microorganism (arsphenamine, or compound 606). Arsphenamine is a derivative of arsenic, and although it could successfully treat syphilis, it did have potentially fatal side effects, which caused it to fall out of use quickly. Shortly after that, in 1928, Alexander Fleming discovered that *Penicillium notatum* mold prevented the growth of *Staphylococcus aureus* and ushered in the era of antibiotic use. Millions of lives have been saved since then by using antibiotics to treat infectious diseases such as pneumonia, sepsis, gangrene, scarlet fever, syphilis, gonorrhea, meningitis, and tuberculosis.

Although plants and natural resources are still used today, they can be a finite resource. The development of new medicines has continued to evolve with the synthesis of drugs in the laboratory and the use of biomolecules or biologics. (Biologics will be discussed in further detail later in this chapter.) There have been tremendous strides in the development of medications that have revolutionized (and will continue to revolutionize) the treatment of disease and our understanding of the human body.

Interdisciplinary Nature of Pharmacology

The nurse administers medication as part of a team that includes other professions. The health care provider (physician, physician's assistant, or nurse practitioner) orders the drug indicated to treat the client. (The term *client* is interchangeable with *patient* in some settings.) The pharmacist evaluates the client and their situation and verifies the appropriateness of the requested medication and its dose for the client. Then, the pharmacist may dispense the medication, recommend the appropriate time for administration, and complete teaching to the client. In the hospital setting, the nurse assesses the client and the potential effects of the medication and then administers the drug after determining the safety to the client. A social worker may become involved if issues of non-adherence to the medication regimen are found or if the client cannot afford the drug once discharged from the hospital. These are just a few of the health care roles involved in the pharmacological care of the client, and often these roles overlap in practice. Communication between professions is crucial in delivering the best care to the client. The concept of collaborative practice, also known as interprofessional (IP) collaboration, within health care professions is viewed as "best practice" because inadequate collaboration may adversely affect the delivery of health care and the safety of the client. More efficient use of resources also results from IP teamwork.

Health care providers should understand each other's roles to prevent mistakes. Competence in interprofessional collaboration is crucial for effective teamwork among physicians, nurses, pharmacists, and others. Interprofessional teamwork improves the efficiency of client care, helps lower costs to the client and the institution, improves client outcomes, and enhances the delivery of holistic care. It also boosts job satisfaction and reduces staff burnout. Maintaining competency includes understanding team goals, having a shared identity, and committing to safe client care while relying on mutual respect and trust. Effective communication and decision-making involves active listening and embracing each discipline's roles in client care.

Pharmacology and Clinical Nursing Practice

Knowledge about pharmacology and the various drugs prescribed and administered to clients is a major part of the nurse's role. Even when not administering the medications directly to the client, it is crucial to the client's care. Nurses must understand the pharmacotherapeutic effects of the drugs in their clinical practice. Drugs have intended or **therapeutic effects**—these are effects that are expected and desired from that particular medication. However, drugs may also have undesirable **adverse effects** or **side effects**.

There are thousands of drugs on the market. Although the nurse is usually responsible for a much smaller number of medications in a specialty area, it is still a significant task to be responsible for the consequences of administering several drugs to various clients with an assortment of diseases. A few of the nurse's responsibilities as they relate to medication administration are listed here (also see Drug Administration for additional information):

- Incorporating the nursing process (assessment, nursing diagnoses, planning, implementation, and evaluation) and clinical judgment into medication administration
- Knowledge of the client and their disease process (or the prevention of disease)
- Knowledge of the drug's name (both generic and brand [trade] names)
- Understanding the indication for the drug (why the client has been prescribed this drug)
- Appropriateness of the drug ordered by the provider
- Assessment of the client prior to administering the drug
- Determining which focused assessments show that the drug is safe for each client
- Understanding which abnormal lab values would prohibit this drug from being given to a specific client
- Special considerations:
  - Life phase (e.g., pediatric, pregnancy, or geriatric populations)
  - Body weight
  - Nutritional status
  - Pathophysiology of the disease process
  - Race and ethnicity
- Determining the safety of the drug in the client
- Contraindications to the use of a drug in a particular client
- Administering the drug(s) using the seven "rights," which are as follows:
  - Right client
  - Right medication
  - Right indication
  - Right dosage range and rate of administration (if appropriate)
  - Right route
  - Right time
  - Right documentation
- Monitoring for potential drug interactions
- Assessment of the therapeutic and adverse effects of the drug
- Education of the client and family (or caregivers) about the disease process, drugs prescribed, and therapeutic and adverse effects

Follow-up with the client is critical to their safety and well-being. The nursing care plan will need to be modified if goals are not reached, and this may need to be done in collaboration with other health care team members. Communication between interprofessional team members is key to preventing **adverse drug events**. The nurse should allow plenty of time to counsel the client about the prescribed drugs and speak clearly, using simple language that avoids medical jargon. It is helpful to have the client repeat the instructions back to the nurse to assess understanding.

1.2 Drug Sources, Forms, and Names

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 1.2.1 Discuss drug sources and forms.
- 1.2.2 Explain drug standards.
- 1.2.3 Discuss the U.S. Food and Drug Administration's drug approval process.
- 1.2.4 Define the chemical name, generic name, and trade name of drugs.
- 1.2.5 Explain the difference between a drug's generic and brand name equivalents.
- 1.2.6 Differentiate between prescription and over-the-counter drugs.
- 1.2.7 Compare and contrast traditional drugs, biologics, and alternative and complementary drug therapies.

Drug Sources and Forms

Drugs are substances or compounds that prevent, treat, diagnose, or cure various conditions or diseases. As mentioned previously, drugs come from a variety of resources—plants, animal products, and inorganic substances. Ideally, these chemicals have desirable therapeutic effects without harmful properties, although many derivatives may have poisonous effects, depending upon the dosage used. Some plant-based products in use today include digitalis from the foxglove plant, vincristine from the periwinkle, and morphine from the poppy plant. The Amazon Basin is home to countless numbers of plants with medicinal properties. Though not in use today, one of the first paralytic agents used in anesthesia was curare, made from a vine known as *Chondrodendron tomentosum*, found near the Amazon River in South America. The Indigenous population in the area placed a curare mixture on the tip of blow darts and used it for hunting (see Figure 1.3). The prey is paralyzed once curare enters the bloodstream; however, the meat is safe to eat because it is not toxic when eaten and digested.

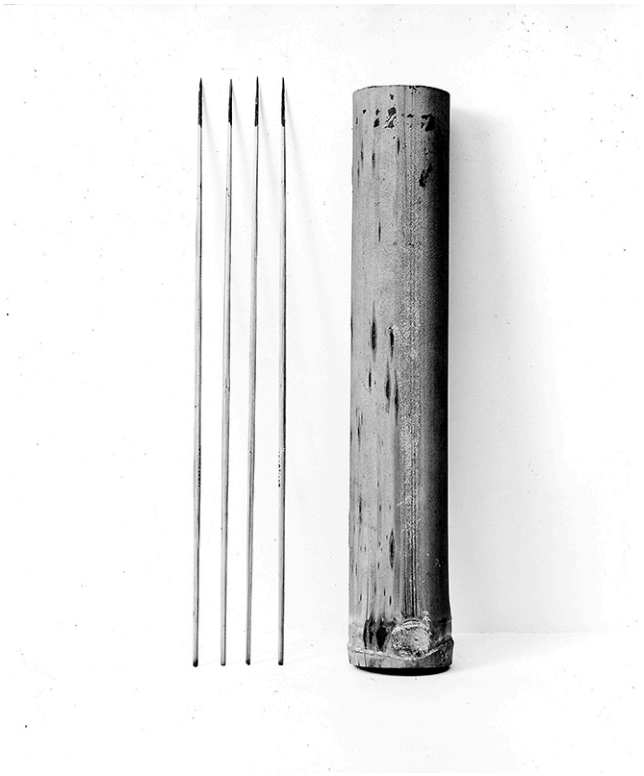


FIGURE 1.3 One of the first paralytics used in anesthesia was curare, which Central American, South American, and Caribbean hunters used to coat blow darts. (credit: "Blow gun darts tipped wih curare from South America"/Wellcome Collection, CC BY 4.0 International)

Some medications come from animals and animal products, including the human body. This list includes a few common medications derived from animals or animal products, though it is not all-inclusive. Heparin and enoxaparin, anticoagulants used to prevent or treat blood clots, are made from pig intestines, and some thyroid medications and pancrelipase are also porcine derivatives. Conjugated estrogens, used to treat menopausal hot flashes, are made from the urine of female horses. Exenatide, used to treat type 2 diabetes, can be made from the saliva or venom of the Gila monster, which is a venomous lizard native to the southwestern United States and northern Mexico. Other drugs come from chicken eggs or yeast.

Several medications, such as vaccines, antivenins and antitoxins, hormones, and monoclonal antibodies, are known as **biologics**. Biologics are medications that come from a living source and are developed through a combination of biomolecular science, immunology, and genetic engineering. Gene-based therapies are another example of cutting-edge research in the world of biologics. They show great promise in treating some cancers and other conditions that currently have no available treatments. They are produced through biotechnological processes, some of which may have unique drug-delivery systems (Atkinson, 2022). Biologics offer the advantage of more targeted therapy for specific diseases, such as autoimmune disorders and cancer, with the potential for fewer side effects, but they are uniquely formulated with complex pharmacotherapy and may require administration through infusions or injections, which adds to the cost of treatment. Monoclonal antibodies, exemplified by etanercept (Enbrel), a biologic, have

revolutionized the treatment of diseases like rheumatoid arthritis (RA). Formerly managed with drugs like methotrexate and corticosteroids, known for their severe adverse effects, monoclonal antibodies now offer a more favorable and less toxic treatment option for RA.

One of the primary drawbacks to the use of biologics is their expense. These drugs take more work to purify, process, and produce, and many are given through infusions or injections. As their patents expire, however, biosimilars may be produced. **Biosimilars** are synthetically produced drugs with similar properties, including mechanism of action and dosing, to those of a biologic. Generally, this allows a biosimilar drug to be produced at a reduced cost than the equivalent biologic drug. Biosimilars are effectively a means to improve the access to biologics while decreasing the cost of therapy.

Biosimilars differ somewhat from generic drugs. The development of biosimilars may take as long as 10 years and cost close to $100 million (Pfizer, 2021). Generic medications are much less costly ($1–2 million) and may be developed over only a couple of years. However, the essential difference between a biosimilar and a generic medication is in the drug's molecular structure. Biosimilar drugs have a larger and more complex molecular structure than generic drugs and are made from a living organism such as yeast or bacteria (U.S. Food and Drug Administration [FDA], 2022c). They are not bioequivalent, however, because of the complex manufacturing processes involved. A brand biologic may be produced using a specific cell line or protein to yield the molecule, which is not available to the maker of the biosimilar. They must come up with their own manufacturing process to create a molecule that is very similar. A company manufacturing a generic drug has to demonstrate that the drug is bioequivalent to the brand-name drug, whereas a company developing and producing a biosimilar drug must demonstrate that it is similar to the biologic it is patterned after (called the reference drug). (See more about generic drugs a little later in this chapter.)

Chemical compounds produced in a laboratory either commercially by a drug manufacturer or illegally by individuals producing drugs for illicit reasons are called **synthetic drugs**. The first synthetic drug, a sedative-hypnotic drug known as chloral hydrate, was first used in medicine in 1869. Sometimes scientists will genetically engineer bacteria or slightly alter the chemical structure of substances to produce chemicals that are therapeutic. A small change in the chemical structure of some medications may make them more helpful than they previously were—they may become more potent or have fewer side effects—making the new compound much more desirable. Often individuals have fewer allergic reactions to synthetic drugs.

Many drugs come from inorganic compounds. Inorganic compounds are often salts from chemical components that have been found to have therapeutic effects. Aluminum and magnesium compounds are helpful in the treatment of indigestion, constipation, or diarrhea. Fluoride and iodide strengthen the enamel on teeth and prevent cavities. Iron helps treat iron-deficiency anemia.

Drugs come in many forms, but there are three primary categories for their routes of administration:

1. **Percutaneous administration**: The application of medications to the skin or mucous membranes
2. **Enteral administration**: The administration of medications into the gastrointestinal (GI) tract
3. **Parenteral administration**: The administration of drugs somewhere other than the GI tract (usually this means by subcutaneous, intramuscular, intradermal, or intravenous injection)

Drug forms in the percutaneous category include creams, topical ointments, powders, dressings (such as those used for wound care), and transdermal patches or disks. Other drugs in this category include eye, nose, or ear drops; vaginal medications; and aerosolized liquids that are inhaled and can be absorbed in the lungs. Some drugs in this category are able to deliver the medication in a constant amount over a specific time frame. The therapeutic effects may last longer depending upon the delivery method.

Enteral medications are drugs administered into the gastrointestinal (GI) tract. This can be done orally, rectally, or through a tube in the GI tract. The most common forms for these routes are through capsules and tablets (both may be sustained release), caplets, elixirs, emulsions, lozenges, suspensions, and syrups. The onset of action of these preparations will vary depending upon the form of the drug. Time-release capsules or tablets and enteric-coated tablets should not be crushed or chewed. Generally, these capsules should also not be opened and emptied onto food because this will alter how quickly the drug is absorbed. Note that some formulations can be opened in this manner, but it is best to ask before attempting this. An overdose of medication could result, although a

subtherapeutic dose could also result from opening the capsule.

The parenteral route commonly refers to drugs given by injection, though parenteral literally means "outside the GI tract." The onset of action is often more rapid than with oral administration; however, the duration of action is usually shorter. Because these drugs do not have to travel through the stomach and be metabolized in the liver, the dose is usually smaller than with oral dosing. This route is often prescribed when it is necessary to deliver a drug quickly. It is also helpful when the client is experiencing nausea or vomiting. The drug form for parenteral medications is that of a liquid. There are no barriers to absorption for **intravenous** medications because these drugs are injected directly into the bloodstream—absorption is immediate and complete. **Intramuscular injections** and **subcutaneous injections** may be absorbed rapidly or slowly, depending upon the solubility of the drug and blood flow to the injection area. Drugs that are highly soluble in water are absorbed very quickly (10–30 minutes); however, poorly soluble drugs will be absorbed at a much slower rate.

Drug Names

One of the biggest challenges when learning pharmacology is that all drugs have multiple names and ways to be identified. There are three basic methods for identifying a drug—the chemical name, the generic name, and the **brand name**, or trade name. If more than one drug company supplies a drug to the market, then that drug will have more than one brand name. To further confuse things, these names may vary in different countries.

Chemical names are built around the drug's specific chemical structure or composition. This name usually has little meaning for the nurse, though it does have meaning for the chemist or pharmacist. The chemical names are usually complex and quite hard to pronounce; for example, the chemical name for ibuprofen is 2-(4-Isobutylphenyl) propanoic acid. Most nurses will not use chemical names, though a few, like sodium chloride, which is easy to remember and pronounce, have made it into the nurse's lexicon.

Generic names, also known as common names, are given by the U.S. Adopted Names Council. Often generic names are part of the chemical name's structure, which helps identify and classify the drug. Though these names are usually easier to remember than chemical ones, they can still be difficult to pronounce. There is only one generic name for each drug, and many organizations worldwide use the generic name for identification, so students are encouraged to learn the generic names when learning about drugs. Though brand names are frequently used in the clinical setting, generic names are preferred for safety reasons. Generic names are also incorporated into the National Council Licensure Examination (NCLEX); therefore, it is helpful to learn the generic names of medications before sitting for a licensure exam.

A brand name (or trade name) is created by the drug company and marketed to providers and consumers. Usually, these names are much easier to pronounce and remember, so they are frequently used in the clinical setting. More than one drug company may produce the same drug. The generic name will be the same, but the brand name will differ. For example, ibuprofen is the generic name for a common nonsteroidal anti-inflammatory drug. Johnson & Johnson manufactures and sells ibuprofen under the brand name Motrin; however, Haleon produces and sells ibuprofen under the brand name Advil. Note that the drug's brand name begins with a capital letter, but the generic name does not (see Figure 1.4).

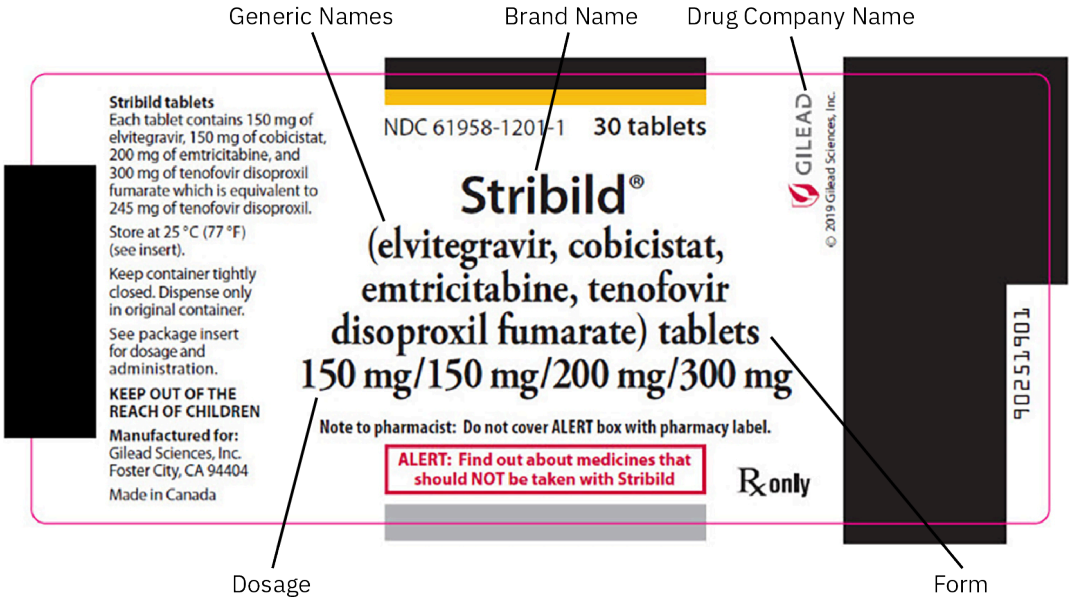


FIGURE 1.4 The basic content of a drug label includes the drug brand name, drug company name, generic names, dosage, and form of the medication. (credit: modification of work "STRIBILD- elvitegravir, cobicistat, emtricitabine, and tenofovir disoproxil fumarate tablet, film coated" by National Library of Medicine/DAILYMED, Public Domain. Drug Company Logo All Rights Reserved.)

Generic and Brand Name Drug Equivalents

When a pharmaceutical company first creates a drug, it is developed as a specific chemical substance. This substance is subject to approval by the U.S. Food and Drug Administration (FDA) once it has undergone rigorous testing with both animal and human subjects. Once approved by the FDA, the pharmaceutical company is given a patent for the drug for several years and it is sold under a brand name chosen by that company.

It is common for drug companies to have entire teams dedicated to the naming of drugs, and that process can be quite lengthy, even as long as four years. Pharmaceutical companies want names that are easily recognizable by both the public and the prescriber. Unfortunately, many drug errors occur each year due to the similarity of the names of drugs (e.g., dopamine and dobutamine or prednisone and prednisolone).

Because there is no market competition for a new drug initially, the cost of it is usually relatively high. Once the patent expires, however, any pharmaceutical company can then make the same drug for sale. Some companies exist to manufacture only generic medications, and they, too, are subject to FDA approval; however, they usually do not have the research and development protocols that the original company did. That is why generic drugs are less expensive than brand-name preparations. Most generic drugs today are formulated in a way that makes them almost identical in effectiveness to their brand name equivalent. According to the FDA (2021a), a generic drug is manufactured with the intent that it is identical in the active chemical ingredients, safety, strength, quality, dosage form, and intended use as its brand name counterpart. Drug formulations are sometimes different because some of the inert substances within the drug may differ between companies, which may affect absorption. It is unclear whether all generics match the brand name drugs they are to represent—the answer is probably not. The thing to remember is that rigorous testing must be performed to show that the generic drug form behaves in the human body in a similar manner to the brand name that it is patterned after—if it does not, it will not be approved by the FDA. Companies that manufacture generic drugs must test to ensure equivalency, but they do not have to redo the efficacy trials. This is where the cost savings of a generic drug occur.

Prescription and Over-the-Counter Drugs

Prescription medications are drugs available to the client only by an order (commonly known as a prescription) from a health care provider. The health care provider must have the training and license to prescribe the drug. The prescription communicates the provider's plan for the client and drug to the nurse or the pharmacist. Originally prescriptions were written using Latin terminology. R_X is an abbreviation of a 14th-century Latin term for recipe that meant "take." Some of the Latin terms continue today, though the use of apothecary terms, such as grains, minims, and drams, is discouraged in practice for safety reasons. (See Drug Administration for more about the various systems of measurement.) Although prescription laws vary slightly from state to state, most require the following

information (see Figure 1.5):

- Name, address, and phone number of the prescriber
- Date (and time, in some settings) the prescription was written
- Drug Enforcement Administration (DEA) number of the prescriber for controlled substances
- Client identification (name and date of birth)
- Client address
- Drug name and dosage strength with the number of dosage units to be prescribed
- Number of refills
- Prescriber's signature

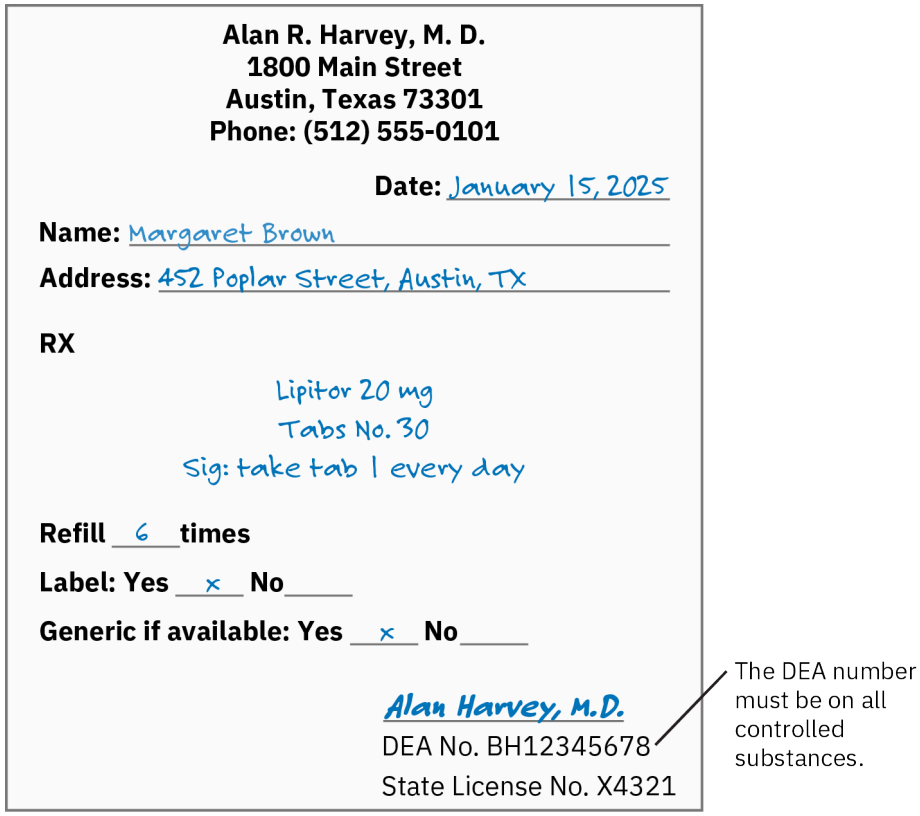


FIGURE 1.5 This sample prescription shows the required elements. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Over-the-counter (OTC) drugs are available without a prescription to the public. They usually are safer than prescription products and are available for self-medication for various ailments. As long as the consumer follows the directions on the label, OTC drugs are usually safe and effective if used for a short time (FDA, 2018b). Some prescribers believe that allowing consumers to buy OTC drugs to treat minor illnesses permits individuals with more serious problems to be seen by the health care provider. However, it is also possible that by taking an OTC drug, the symptoms of a serious disease might be hidden or treatment delayed.

There are over 80 classes of OTC drugs, including pain and fever reducers, laxatives, antidiarrheals, and cold, cough, and allergy medications. Occasionally drugs are originally developed and sold only under prescriptive authority; however, after a period of time and with many clients using the drug, it is determined that it is safe for nonprescription use as an OTC. All OTC drugs are regulated and evaluated under the supervision of the FDA.

Over-the-counter drugs may still carry risks to the client. They are safe only if taken as recommended on the drug label. At times, consumers may inadvertently take more than the prescribed dose of an OTC due to taking more than one drug with the same product in it. The prescription medication Norco, for example, contains hydrocodone and acetaminophen. If taken with Tylenol (which also contains acetaminophen), the client may ingest more than the recommended dose of acetaminophen. The use of OTC drugs can be harmful in clients with some chronic diseases, such as diabetes, and those with liver or kidney problems. For example, acetaminophen is only safe when taken

within the prescribed dose of fewer than 4 grams (4000 milligrams) per day—less should be taken if the client is older, malnourished, or has liver problems.

Many clients do not consider OTC drugs as medication and will not always report the use of these drugs. When taking a drug history, listing all dietary supplements and OTC drugs is crucial to prevent interactions.

Even though the cost of OTC medications is usually lower than those of prescription drugs, the cost of the OTC drugs is often incurred directly by the client. Insurance companies do not usually cover the cost of OTC medications.

This section would not be complete without a mention of **complementary and alternative medicine (CAM)**. Medications are often used to treat clients in the Western world; however, other approaches are used outside the conventional treatment seen in Western medicine. Several of these were first developed in the Far East. Alternative medicine refers to using a treatment *instead of* mainstream conventional medicine, whereas complementary therapy refers to using *both* alternative medicine and conventional medicine together. These treatments may include massage, acupuncture, acupressure, mind–body interventions, or dietary supplements such as herbs or vitamins. One common use of CAM is in the treatment of cancer. Many drugs used to treat cancer have side effects of severe nausea and extreme fatigue. CAM may help clients cope with these symptoms through the use of acupuncture or the use of ginger or peppermint. Herbal therapy is also quite popular, but various herbals can interact with mainstream medications such as digitalis and blood thinners. St. John's wort is an herbal supplement that interacts with drugs in the class of selective serotonin reuptake inhibitors and has the potential to cause a potentially fatal condition known as serotonin syndrome. Obtaining a list of herbals and supplements is vital when assessing a client's medications. Herbals and supplements are not subject to FDA approval, and the supporting evidence for the use of these substances is low to nonexistent.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Vy Min is a 34-year-old client who presents to her health care provider's office with reports of a headache, cough, and sharp right-sided chest pain during deep inspiration and coughing. The client states she has been taking acetaminophen 1000 mg every 4 hours for the last 48 hours and dextromethorphan 2 teaspoons every 4 hours, as needed, for coughing.

History
Seasonal allergies
Indigestion

Current Medications
Cetirizine 10 mg orally daily
Dextromethorphan (Robitussin) 2 tsp orally every 4 hours as needed for cough
Acetaminophen 1000 mg orally every 4 hours for 48 hours
A small red pill (taken for indigestion, she doesn't recall its name)

Vital Signs		Physical Examination
Temperature:	100.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; no peripheral edema noted bilaterally; S1, S2 noted • *Respiratory:* Right-sided crackles posteriorly • *GI:* Abdomen soft, nontender, nondistended • *GU:* Reports normal urine output
Blood pressure:	118/66 mm Hg	
Heart rate:	90 beats/min	
Respiratory rate:	18 breaths/min	

TABLE 1.1

Vital Signs		Physical Examination
Oxygen saturation:	95% on room air	
Height:	5'1"	
Weight:	102 lb	

TABLE 1.1

1. Vy states that she has been taking 1000 mg of acetaminophen every 4 hours per day for the last 48 hours. What is the priority nursing intervention for the client?
    a. Draw liver enzymes immediately.
    b. Educate the client about dosage recommendations for acetaminophen.
    c. Notify the health care provider to recommend initiation of hydrocodone.
    d. Immediately assess the client's bowel function.

2. The nurse is discussing the use of over-the-counter medications with Vy. What advantages of using over-the-counter drugs will the nurse discuss?
    a. Over-the-counter drugs do not need to be reported to the provider.
    b. Insurance companies will reimburse the cost of over-the-counter medications.
    c. Minor ailments can be treated by the client rather than the prescriber.
    d. Over-the-counter drugs are always safe.

Drug Standards

The FDA is the government agency responsible for the regulation of the development, production, and sale of drugs. The FDA was given much closer control over the production of drugs after the drug thalidomide was prescribed to pregnant clients for the treatment of morning sickness and for sedation in the 1950s and 1960s. This drug was found to be highly **teratogenic** to fetuses and caused many fetal malformations, especially limb defects. The Kefauver-Harris Amendments in 1962 required drug manufacturers to establish the efficacy of drugs and gave the FDA more control over the testing of drugs before they were placed on the market.

The United States Pharmacopeia National Formulary (USP-NF) has a rich history, dating back to the inaugural publication of the *United States Pharmacopeia* in 1820. In 1888, the National Formulary (NF) joined its ranks. Then, in 1975, these two entities merged to form the formidable USP-NF. This institution operates as an independent, nonprofit organization dedicated to establishing vital standards for compounding medications, biologics, drug development, and manufacturing, both within the United States and globally. It produces the only *official* book of drug standards in the United States annually, and drugs referenced in this book have met very high standards for quality, strength or potency, and purity (U.S. Pharmacopeia, n.d.). The USP-NF is a nongovernment organization and is not associated with the FDA; however, the standards that the USP-NF puts forth are enforced by the FDA as the official standards for the production and quality control of drugs and dietary supplements in the United States. Complementary medications and supplements are not required to meet these same standards, though some do, and they carry a USP seal guaranteeing safe manufacturing and quality. The Canadian Food and Drugs Act also recognizes the USP-NF as a reliable authority of drug standards in Canada for health care providers.

There are many reliable sources of drug information for health care providers, including the American Society of Health System Pharmacists' *AHFS Drug Information* book and *Drug Facts and Comparisons.* Many online resources are available to nurses, such as Medscape (https://openstax.org/r/medscapeorg), Skyscape (https://openstax.org/r/education), DailyMed (https://openstax.org/r/dailymeda), and UpToDate (https://openstax.org/r/wolterskluwer). Applications can be downloaded to personal electronic devices or devices in the clinical setting (though not all are free). Often hospitals/health care systems and clinics have institutional access to these resources. It is helpful for the nurse to be able to access a wide variety of resources. A useful and free app for herbal supplements is *About Herbs* (https://openstax.org/r/mskcc), which is produced by Memorial Sloan Kettering Cancer Institute. It is particularly helpful in the discussion of the mechanisms of action, herb–drug interactions, and adverse effects.

Drug Approval Process

The Center for Drug Evaluation and Research (CDER) is a branch of the FDA that evaluates new drugs before they can be sold in the United States. It provides health care providers and consumers with the information needed to use drugs appropriately. One of the tasks of CDER is to ensure that both brand-name and generic drugs work as they should (FDA, 2022b). Before any drug is sold in the United States, it must be tested. Once a chemical that may have therapeutic effects is isolated, it will undergo scientific tests and clinical trials to prove its efficacy and safety. Drugs must pass through several stages of development before receiving approval from the FDA to be marketed to consumers. Table 1.2 briefly describes the process of obtaining FDA approval for a new drug.

Stage of Development	Description
Preclinical trials	Drugs are tested on animal subjects to evaluate the compound in living tissues and to evaluate for adverse effects.
Phase I studies	A very small sample of human volunteers is used to test the drugs. Usually, the individuals are healthy subjects.
Phase II studies	Clinical investigators test the drug on clients with the disease that the drug has been developed to treat. Subjects are monitored very closely to evaluate the intended effects and for adverse reactions.
Phase III studies	This is a large-scale clinical trial. Prescribers assist in observing the client taking the drug. The goal of this phase is to gather data about the effectiveness and safety of the drug.
FDA approval	Once drugs make it through Phase III studies, they are evaluated by the FDA following the submission of a New Drug Application. If the FDA approves the drug, it can then be marketed.
Phase IV studies (post-marketing surveillance)	Continual evaluations of drugs following approval by the FDA

TABLE 1.2 **Summary of the Phases of Drug Development**

Some estimate the cost of developing just one new drug as ranging from less than $1 billion to over $2 billion (Wouters et al., 2020). The development of new drugs requires 10–15 years before the testing and drug studies are complete. Thousands of compounds are tested yearly, but only a few make it to clinical trials. Once a drug enters clinical trials, only a few are approved. CDER does not perform the clinical trials—this is up to the drug company; however, CDER reviews the pharmaceutical company's data and the proposed drug labeling. At the heart of the approval process is establishing the health benefits of the drug and its safety profile. Does the benefit of the drug outweigh its risk?

There also are limitations to testing new drugs. Historically, there has been limited testing of drugs in the populations of females (particularly those of childbearing age), children (anyone under the age of 18 years old), and people of color (POC). This has recently changed, but before 2000, minimal testing was performed on females. No clinical trials were allowed for females of childbearing age, even if they were not pregnant and were taking effective birth control. This greatly limited knowledge about how females would respond to many drugs. This also means that there is limited data about drug safety during pregnancy.

Children were also excluded from clinical trials in the past, though some exceptions have been made more recently. According to the FDA (2016), only about 20% of drugs are approved for pediatric use. For that reason, physicians have had to prescribe drugs "off-label" for children. The problem is that well-controlled clinical trials for pediatric dosing have not been established for many drugs, meaning there is no safety data for most drugs. The reasons for this lack of data are somewhat surprising. Some believe that pharmaceutical companies saw little profit in medications for children. Finding adequate numbers of children for robust testing could be more of a challenge than with adults, especially in trials where blood would need to be drawn.

There are also ethical reasons to exclude children from trials, especially because children are unable to give consent. According to the FDA (2016, para. 7), "Parents are involved in the decision to enroll children in a study, and

children ages 7 or older can 'assent' or 'dissent,' meaning they can agree or disagree to participate in a study." For more information about children's assent and parental permission, review this article by the National Cancer Institute (https://openstax.org/r/cancera). More testing has been conducted in the last decade, and the information coming out of those studies has shown much more accurate methods for dosing and prescribing. The FDA web page on drug research and children (https://openstax.org/r/fda) has more information.

LINK TO LEARNING

Clinical Trials for Children

Access multimedia content (https://openstax.org/books/pharmacology/pages/1-2-drug-sources-forms-and-names)
In this video from the National Heart, Lung, and Blood Institute, pediatric researchers, doctors, and nurses explain why children should be included in clinical drug trials and answer common questions from parents and caregivers.

Even as late as 2019, only 15%–19% of participants in U.S. clinical drug trials were Black. When broken down further, only 3% of participants in clinical trials for cardiovascular disease were Black males (6% were Black females), and less than 5% of oncology trial participants were Black males (2% were Black females) (Whyte, 2022). When specific populations are under-represented in a clinical trial, the efficacy and safety are unknown for that particular subset. The efficacy and safety of some drugs may differ for various ethnicities and genetic backgrounds (Clark et al., 2019). Due to a variety of barriers, racial and ethnic minorities are often underrepresented in clinical trials (FDA, 2022a). When clinical trials test therapies only within a homogenous group, the findings are likely to be skewed. One of the problems with this is that minority groups may have less benefit from those therapies. Some of the barriers to increasing minority involvement in clinical trials include a lack of understanding of the value of the process; mistrust of research; lack of information, time, and resources; and a lack of knowledge about the existence of various trials (Clark et al., 2019). Many differences in health outcomes have been documented based on race and ethnicity, underscoring the importance of including a variety of racial and ethnic groups in clinical trials.

TRENDING TODAY

Off-Label Prescription Drug Use

Access multimedia content (https://openstax.org/books/pharmacology/pages/1-2-drug-sources-forms-and-names)
Off-label prescription drug use pertains to the utilization of a medication in ways that deviate from the specifications provided on the drug's label or within its FDA-approved package insert. Such usage encompasses employing the medication for divergent medical conditions, adjusting dosages, targeting varying client groups, or employing alternative routes of administration, all of which may contrast with the medication's initial FDA approval. For example, after the COVID-19 pandemic started, a research institute focused its efforts on repurposing existing drugs (see the Wyss Institute website (https://openstax.org/r/harvard) and the video above).

Access multimedia content (https://openstax.org/books/pharmacology/pages/1-2-drug-sources-forms-and-names)
The safety of off-label drug use varies based on factors such as the specific medication and condition, the health care provider's judgment and knowledge, and the available evidence. Providers should weigh potential benefits against risks (as discussed in the *Wall Street Journal* video above) because off-label use may be valuable when approved alternatives are lacking. This article provides 2023 statistics on the drug classes (https://openstax.org/r/ncbia) in which off-label use is typical.

When administering off-label drugs, nurses should ensure informed consent from the client or their representative, discussing potential risks and benefits of the proposed medication. The nurse should also collaborate with the health care team for guidance and to determine the appropriateness of the drug. Other duties of the nurse include documenting the rationale for the use of the drug, educating the client on its proper use, monitoring the client closely for unexpected effects, and staying updated on the latest research. Above all, it

is important for the nurse to uphold ethical principles and keep the client's well-being at the forefront.

Canadian Drug Regulation

The United States' and Canada's drug laws have evolved in a similar manner. Any drug manufacturer must provide scientific evidence of the drug's safety, efficacy, and quality to Health Canada before the sale of that product is authorized. The federal review process by Health Canada was empowered by the Food and Drugs Act of 1927 as well as additional regulations (in 1953, 1954, and 1979) intended to protect consumers from risks associated with the production and sale of drugs, cosmetics, food, and medical devices (Health Canada, n.d.). It regulates the manufacturing, packaging, labeling, storage, and sale of food and drugs in Canada. It also determines whether a drug is a prescription or nonprescription medication. Canada requires prescriptions for narcotics and strict guidelines for record-keeping for prescribing and dispensing those drugs. Drug use in Canada is regulated and enforced by many different agencies, including Health Canada, the Royal Canadian Mounted Police, and agencies within various provinces.

Although the schedule of drugs is different from that of the United States (see Drug Classifications and Prototypes for U.S. drug schedules), Canada has tried to align the schedules throughout each province so that the sale of medications is consistent throughout the country. The governing body for Canadian national drug schedules is the National Association of Pharmacy Regulatory Authorities (NAPRA), though each province does regulate how drugs are sold or dispensed. In Canada, drugs are assigned to one of four categories (Drug & Alcohol Testing Association of Canada [DATAC], 2017; National Association of Pharmacy Regulatory Authorities, 2023):

- *Schedule I:* All prescription drugs. These drugs must be provided to the consumer by a pharmacist through a controlled, regulated environment. Drugs in this category include heroin, cocaine, morphine, and methadone.
- *Schedule II:* Restricted-access nonprescription drugs. These drugs may require professional intervention from a pharmacist when sold to the consumer. Must be stored with no public access or chance for the public to choose or select the drug (in other words, "behind the counter"). Schedule II drugs include insulin, pseudoephedrine, and sublingual nitroglycerin.
- *Schedule III:* Available without a prescription and sold on store shelves under the supervision of a pharmacist. Examples in this category are ibuprofen or naproxen.
- *Unscheduled:* Can be sold without supervision from any retail outlet. Emergency contraception, such as norgestrel, is considered an unscheduled drug.

Drug Counterfeiting

The United States has one of the world's safest drug supplies, partly due to the FDA and USP-NF. Unfortunately, counterfeit drugs threaten that safety. **Counterfeit drugs** are products that are illegally manufactured or mislabeled with regard to their identity or source so that they appear to be a genuine product. They are fake drugs and may harm the recipient's health. Illegal online sales expose consumers to potential counterfeit drugs. Counterfeit drugs are not the same thing as generic medications. As mentioned earlier in this chapter, a generic drug is manufactured with the intent that it is identical in the active chemical ingredients, safety, strength, quality, dosage form, and intended use as its brand name counterpart (FDA, 2021a). These are drugs approved by the FDA. Counterfeit drugs are not.

Consumers can protect themselves by buying medications from state-licensed pharmacies in the United States. If using an online pharmacy, the consumer should check for the online pharmacy's license through the state Board of Pharmacy. If it is not listed, that pharmacy should not be used. Reputable online pharmacies should have a seal of approval from the Verified Internet Pharmacy Practice Site (VIPPS). An online pharmacy should always require a health care provider's prescription and have a physical address and phone number in the United States. Another strategy for the consumer is to be alert to changes or variations in the packaging of medications—for example, the color or lettering might be different. Consumers should be alert to any unusual taste or side effects from the drug and report it immediately. Concerns about potential counterfeit drugs should be reported to the FDA through its MedWatch website (https://openstax.org/r/fdag) or by calling 1-800-FDA-1088. The 2013 Drug Supply Chain Security Act was passed as an initiative to combat the production and use of counterfeit drugs. The FDA's Office of Criminal Investigations investigates counterfeit drugs, their producers, and their sellers and attempts to bring them to justice.

1.3 Drug Classifications and Prototypes

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 1.3.1 Explain the basis for placing drugs into therapeutic and pharmacologic classes.
- 1.3.2 Discuss the prototype approach to drug classification.
- 1.3.3 Define federal controls on drugs that have abuse potential.

Drug Classifications

One helpful method for sorting out the sheer number of drugs on the market is by organizing them into different classifications. Most drugs are classified in two ways—therapeutic classification and pharmacologic classification.

- **Therapeutic classification** refers to a drug's therapeutic use or clinical indication (the diagnosis or disease being treated). When using a therapeutic classification, one describes the therapeutic effect, or the clinical result that occurs after the client takes a drug. For example, in Antihypertensive and Antianginal Drugs, the drug metoprolol is discussed. Its therapeutic classification is antianginal because it relieves the chest discomfort associated with coronary artery disease. It also reduces blood pressure, so it has a second therapeutic classification and is also known as an antihypertensive.
- **Pharmacologic classification** refers to *how* the drug works in the body—its mechanism of action. Metoprolol's pharmacologic classification is beta-adrenergic blocker—it works by blocking the stimulation of the body's beta-adrenergic receptors, which inhibits the heart's response to sympathetic nerve stimulation. Sometimes a drug is classified by the body system it affects, such as the autonomic nervous or upper respiratory systems.

Important note: Even though a drug may have more than one therapeutic classification, such as the previous example of metoprolol being both an antianginal and an antihypertensive, it will essentially have the same mechanism of action (though its targeted effect may be different), side effects, and safety parameters. Knowledge of a drug's classification helps the nurse understand its intended effects and its adverse effects. The primary difference is in the client's reason for taking the drug.

Drug Prototypes

Once drugs are sorted into classifications, it is customary to utilize one drug within the class to compare to all the other drugs within that class. It becomes the "class representative," known as the **drug prototype**. Using a drug prototype is helpful for an individual learning pharmacology because it makes learning much more manageable. It is also helpful in the clinical setting. Consider the situation of a nurse who has administered the beta-adrenergic blocker metoprolol multiple times in the clinical setting and is quite familiar with its actions and side effects. When a health care provider orders the beta-adrenergic blocker atenolol, that nurse knows it will have a similar mechanism of action, side effects, and safety parameters as metoprolol. This is much easier for the student to learn than attempting to identify and learn every single drug made in the class.

Pharmacology books often use drug prototypes to simplify explanations of drug classes and assist students in their learning. Table 1.3 provides an example of a drug prototype table used throughout this text.

Drug Class Pharmacological class or Therapeutic class **Mechanism of Action** This is a description of how the drug works in the body.	**Drug Dosage** This indicates the quantity, frequency, and route of administering the medication to the client, and how it may differ by age, body weight, or clinical condition.
Indications How is the drug used? What disease or symptom does it treat? Is it used for prevention? **Therapeutic Effects** This explains the drug's desired effects—how the provider knows if it is effective.	**Drug Interactions** Are there any drugs that cause undesired effects if used together? **Food Interactions** Do foods prevent the desired effect from occurring? Do certain foods cause toxicity?
Adverse Effects What undesired effects might occur?	**Contraindications** Is there a reason this drug should be avoided in this client?

TABLE 1.3 **Sample Drug Prototype Table**

Drug Schedules

Many different chemicals, substances, and drugs come under U.S. Drug Enforcement Administration (DEA) oversight (U.S. DEA, n.d.). In 1970, Congress passed the Controlled Substances Act, which led to the establishment of the DEA in 1973 and described the controls for manufacturing, distributing, and prescribing habit-forming drugs. This legislation not only categorized controlled substances based on their potential for abuse but also established drug schedules and provided drug treatment programs for those with addictions. All hospitals and pharmacies must keep records of drugs purchased and sold. Any health care provider with prescriptive authority must be registered with the DEA and given a unique DEA identifier that they must place on any controlled substance prescription.

As noted in Table 1.4, Schedule I drugs have no medical use and a very high potential for abuse and physical/psychological dependency; therefore, most health care providers cannot issue prescriptions for those drugs, and pharmacies cannot fill those prescriptions. If research is being conducted with a Schedule I drug, applications and supporting documents have to be sent to the DEA for special permission. Schedule II, III, and IV drugs must have a medically sound reason for a prescription. Schedule V drugs are those with the lowest potential for misuse and dependency (U.S. DEA, n.d.).

Cannabis has been classified as a Schedule 1 drug since the 1970 Controlled Substances Act. However, more than half of the states in the nation have decriminalized the substance, with some permitting medical usage and others both medical and recreational usage. As of May 2024, the Drug Enforcement Agency has recommended that cannabis be reclassified as a Schedule III drug, which would support wider medical usage and scientific research but not permit recreational usage on a national level. Formal reclassification will require additional steps.

Drug Schedule	Examples of Drugs in This Category	Therapeutic Use	Potential to Cause Physical or Psychological Dependency	Potential for Abuse
Schedule I	Heroin, lysergic acid diethylamide (LSD), peyote; see above regarding cannabis	No accepted medical use	High	The highest potential for abuse
Schedule II	Cocaine, methamphetamine, oxycodone, fentanyl, methadone, hydromorphone, mixed amphetamine salts, Adderall, Ritalin	Medical use	High	High
Schedule III	Acetaminophen with codeine, ketamine, anabolic steroids	Medical use	Moderate to Low	Moderate to Low
Schedule IV	Benzodiazepines such as alprazolam and diazepam; tramadol	Less abuse potential than Schedule III drugs and limited dependence liability	Low	Low
Schedule V	Atropine with diphenoxylate (Lomotil), pregabalin	General medical use	Low	Low

TABLE 1.4 **Scheduled Drugs in the United States** (sources: https://www.dea.gov/drug-information/drug-scheduling; https://americanaddictioncenters.org/prescription-drugs/classifications)

1.4 Special Considerations

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 1.4.1 Discuss the impact of socioeconomic factors on pharmacology.
- 1.4.2 Describe how decisions are made relative to drug therapy and specific groups of clients.
- 1.4.3 Explain how the “silver tsunami” is impacting drug therapy.

Pharmacology and Socioeconomic Factors

Without question, medication costs have been escalating for many years. Many factors encompass total health care costs: the up-front costs of prescription drugs, visits to providers and health care institutions, morbidity and mortality, diagnostic and interventional medicine, and suboptimal medical therapy, to name only a few. Increased drug utilization and increased price factor into this increased health care cost. A larger share of health care costs has been passed on to the consumer in the form of out-of-pocket expenses as health care costs have risen. The field of pharmacoeconomics probes into the analysis of the costs of drug therapy to health care systems and society as a whole, and it examines the consequences of providing pharmacological products and services to clients.

The prevalence of chronic conditions in the United States continues to rise and accounts for the majority of health

care costs (Wilder et al., 2021). Although there are many medications that can treat these conditions, half of all clients do not take their medications as prescribed. A lack of insurance coverage does impact the likelihood of medication non-adherence. So, not only do more chronic medical conditions occur in individuals living in reduced circumstances, but those same circumstances prevent them from managing their care appropriately. The United States has a system of voluntary insurance that does not guarantee the same coverage for all individuals in the country. This is because coverage is expensive and sometimes difficult to purchase. A primary objective of the Affordable Care Act, which was signed into law under President Barack Obama in 2010, was to make it easier for people in the United States to obtain voluntary insurance. Even though it is thought that approximately 92% of individuals in the United States have some type of health coverage, over 27 million individuals are still without coverage (Statista, 2023; Tolbert et al., 2022).

Often an insurance company or a medical institution will have a **drug formulary**. This is a list of prescription drugs that are covered by that plan. The purpose of the formulary is to provide good care while using the most cost-effective medications. Not all drugs will be included on an insurance plan's formulary, meaning the client may be responsible for the cost of specific drugs or switch to an alternative agent. Some insurance plans also have a deductible, which means that the client must pay a certain amount of money "out-of-pocket" before the insurance begins to pay for medications.

TRENDING TODAY

The World's Most Expensive Drug...For Now!

The FDA approved the first gene-therapy drug for hemophilia, a blood-clotting disorder, in November 2022. Hemgenix was developed by the drug company CSL Behring. This particular drug is helpful in treating clients with a factor IX deficiency. Even though only a single dose of the drug is needed to provide protection from severe bleeding for up to 8 years, this drug does not protect those with the most common forms of hemophilia. The cost of a single dose: $3.5 million (Naddaf, 2022).

Costs are calculated based on how much it costs for a pharmaceutical product to be developed and manufactured. Medical visits, treatments, and hospitalizations might be considered a *direct medical cost* to the client. A *direct nonmedical cost* could be the cost associated with out-of-town office visits, such as food and lodging. These are costs associated with medical treatment, but they are not medical in nature. An *indirect cost* involves costs to the client that are associated with the loss of income or productivity because of an illness. *Intangible costs* are due to an illness but are difficult to measure, such as the cost of loss, pain, or suffering.

Medical outcomes also have to be measured. Is the outcome the preservation of life or a cure for the disease? Is the client able to be a productive member of society again? Should a drug company invest in a drug that will cure a rare disease but costs billions of dollars? Who pays for the treatment? Should the drug company invest in a much cheaper drug and help millions of people? That may seem like a simple answer unless you or a loved one are the ones with the rare disease.

SPECIAL CONSIDERATIONS

Socioeconomic Factors

There are many potential reasons for nonadherence to a drug regimen. Socioeconomic factors can prevent the client from receiving the care necessary to prevent disease or restore health. The nurse should identify and investigate barriers to any health care provider or clinic visits, treatments, or needed medication. Use simple, nonjudgmental language to discuss the client's financial concerns. Explore whether the client has health insurance. Collaborate with other disciplines, such as pharmacy or social work, to develop a plan that best meets the client's needs. Many pharmaceutical companies have programs to assist clients who cannot afford their medications.

Drugs as They Relate to Specific Populations

The very young and the very old are predisposed to be the most sensitive to drugs. One factor causing this is the

differences in pharmacokinetics in these individuals. **Pharmacokinetics** is the movement of a drug through the body. It is easiest to think of it as "what the body does to the drug." Drug absorption, distribution, metabolism, and excretion vary with age. The liver and kidneys are immature in very young clients, which significantly impacts metabolism and excretion; however, absorption and distribution of drugs are also impacted by their age and body size. Older adults also experience differences in pharmacokinetics; these are discussed in a separate section later in this chapter. Pharmacokinetics are discussed in more detail in Drug Administration.

Many drugs' absorption, distribution, metabolism, and excretion differ among infants, children, and adults. Most drugs are either metabolized by the liver or excreted by the kidneys, and the rate and level of organ functioning vary between age groups.

Pediatric Population

Developmentally, infants and children have a much smaller body mass; therefore, accurate pediatric dosing is crucial. Pediatric dosing is sometimes calculated by milligrams per kilogram (mg/kg) of body weight or by body surface area (BSA). It is essential to be very accurate when calculating pediatric doses. Math should be double-checked to reduce the incidence of medication errors or inadvertently giving a higher-than-desired dose. The Pediatric Pharmacy Association commissioned several individuals to develop a KIDs List of drugs (https://openstax.org/r/aafp) that identifies potentially harmful or inappropriate drugs in the pediatric population. The KIDs List includes two recommendation levels (avoid and use with caution).

CLINICAL TIP

Pediatric Dose

One safety measure is to give medication to pediatric clients using the smallest syringe available for a specific dose, allowing for a more precise measurement of the drug.

One of the challenges with drugs in pediatric clients is the limited testing when researching the drug. Almost all information about drugs, in general, is related to dosing in the adult client. The risk of performing research in this population and obtaining informed consent makes researching drugs a problem.

Body Size

Another factor that impacts an individual's sensitivity to a drug is body size. The body's response to a drug is often determined by the concentration of the drug at the site of action. The higher the concentration at the site, the stronger the response to the drug; the lower the concentration at the site, the less intense the response. A client with overweight or obesity may require a larger dose to obtain the intended effect, whereas an undernourished client may need a smaller dose. This is one reason that accurate height and weight are so important in the physician's office or clinical setting. Many drugs are calculated by milligrams per kilogram of body weight to obtain the correct dosing for the intended therapeutic effect.

Sex

More research needs to be done regarding how biological differences between the sexes impact the use and metabolism of medication. Male versus female clients may experience a difference in symptomology with certain diseases. There is often a difference in body size, percentage of body fat, and muscle mass. These factors may impact the response to drugs and their effectiveness based on sex. There also is often a difference in how male versus female clients experience the adverse effects of the same drug. In 1977, most individuals assigned as females at birth were banned from many trials. This policy was reversed when Congress passed into law the National Institutes of Health (NIH) Revitalization Act of 1993 (FDA, 2018a). However, although inclusion has increased, the rate of inclusion has been slow, and there is not adequate knowledge about many drugs in regard to how they affect this population.

Pregnancy and Lactation

Pregnancy and lactation are other areas of medicine where researchers exercise greater caution due to the risk of adverse effects of a drug or substance on the fetus. When giving a drug to someone who is pregnant, the provider must consider both the pregnant client and the fetus. In many cases, it is safest to postpone treatment with drug therapy until after the birth of the infant. However, there are times when drug therapy is unavoidable, such as for a

preexisting condition, upper respiratory or urinary tract infections, or the development of a condition such as hypertension or gestational diabetes that may necessitate treatment. In fact, according to Haas et al. (2018), approximately 97% of those who were pregnant took at least one drug during pregnancy. The benefit to the pregnant client and fetus should always be weighed against the risk of treatment. This can be very challenging in clinical practice.

Many physiological changes occur during pregnancy. Pregnancy alters the pharmacodynamics and pharmacokinetics of each drug and impacts the pregnant body's response to the drug. The pregnant client has changes in bowel function, often slowing the time it takes for digestion. Gastric motility decreases, which causes decreased transit time, allowing more of the drug to be absorbed. This, in turn, causes the effects of the drug to be prolonged, and the client may be at an increased risk of toxicity. Cardiac output and uterine blood flow increase. The kidneys, breasts, and skin also have increased blood flow. Renal blood flow is essentially doubled during the third trimester of pregnancy. This results in an increased glomerular filtration rate that causes many drugs to clear the body much more rapidly.

The placenta allows the transmission of substances between the pregnant client and the fetus. Some drugs pass through the placenta to the fetus, though others are blocked. Several factors determine drug passage across the placenta (e.g., lipid-soluble drugs will pass more easily than those bound to proteins). The nurse should always assume that any medication taken during pregnancy can reach the fetus.

The primary concern with any drug during any pregnancy is its risk to the developing fetus. If a drug is known to cause fetal harm through embryonic or fetal development, it is said to be teratogenic. Only a few drugs have been *proven* to be teratogenic, and even though a drug might be a known teratogen, it does not mean that it will always cause harm to every fetus. It is also important to know that having no data on a drug's safety does not mean that the drug may not cause harm—just that there is no *proof*. Even drugs that are generally considered "safe" during pregnancy may carry some risk—no drug can be considered 100% safe to use during pregnancy.

Before 2014, the FDA used an ABCDX system to classify drugs for pregnancy and fetal risk. Drugs in Category A were considered safest for the fetus during pregnancy, with each successive class increasingly more dangerous. Category X drugs were known to be harmful to the fetus. Often these categories were confusing and not helpful to providers and consumers. Many of the limitations of the system came from a lack of data from clinical trials. When there was a lack of data, many of the drugs were placed into Category C. This meant that no clinical trials had been performed in humans, and animal studies either had not been done or showed a risk of fetal harm. Drugs placed under Category C may have been given to pregnant clients for years with few adverse effects. In 2014, the FDA released the Pregnancy and Lactation Labeling Rule (https://openstax.org/r/fdab) and provided new narrative guidance for the labeling of drugs. The rule took effect in June 2015, and all medications currently approved by the FDA should have the new labeling (FDA, 2021b).

These general guidelines should direct the nurse in caring for clients who may be pregnant or lactating:

- Complete a thorough history of illnesses and diseases that might impact the client.
- Complete a thorough history of all drugs (prescribed and/or recreational), herbal and dietary supplements, vitamins, and over-the-counter medications taken by the client.
- Ask the client of childbearing age about signs or symptoms of possible pregnancy.
- Discuss the potentially harmful effects of taking any drug during pregnancy and during lactation.
- Recommend that the client avoid alcohol or smoking during pregnancy and lactation.
- Inform the client that some herbal or complementary and alternative therapies may help with symptoms of pregnancy, but to discuss any treatments with a provider because not all are safe.

(For additional resources about caring for clients who may be pregnant or lactating, see this CDC website (https://openstax.org/r/cdca), which includes information on the NIH LactMed (https://openstax.org/r/ncbib) database.)

Genetics

One of the newest areas of research in pharmacology is **pharmacogenetics**. This area of pharmacology studies the response to drugs based on a client's individual genetics, including therapeutic responses to drugs and the predisposition individuals might have to the adverse effects of a medication. With the identification of the human

genome through the Human Genome Project, much fundamental information about the human body has improved the practice of medicine. This international collaborative project began in 1990 and was finally completed in 2003. However, it was not until 2022 that the Telomere-to-Telomere consortium finally announced that it had filled in the gaps from the original project and produced the first complete human genome sequence (National Institutes of Health, 2022).

We now know more about heredity and the disease process, and there is growing evidence about the influence of genetic variations on drug response. Often two clients will respond differently to the same drug. This research may help identify genetic variants in the response to drugs that may be unique to a race or ancestral group. Genetic variations can change the structure of drug receptors and target molecules, which can then influence an individual's response to a specific drug. At some point in the near future, clients will benefit from customized drug therapy specific to their genetics. It will predict the best drug for use in a particular situation and allow the dose to be prescribed that best limits side effects or toxicity.

SPECIAL CONSIDERATIONS

Cultural Concerns

There are cultural considerations that the nurse must integrate into the care of the client:

- Acknowledge individual differences.
- Reflect on one's own potential inherent biases.
- Practice cultural humility.
- Embrace and respect diversity.

Accommodating the culturally diverse:

- Assess their ability to communicate.
- Engage an interpreter if the client's use of English is limited.
  - Avoid using a family member to translate when possible.
- Provide health information to the client and family members in their primary language, when possible.
- Assess the client's current health practices.
- Determine whether cultural healers are important to the client.
- Obtain a complete history of the client's medications and use of herbals, OTCs, vitamins, and CAM.
- Determine the client's views about touch, eye contact, and modesty.
- Recognize that various cultural and biological responses may occur within different groups.
  - Black clients may not respond to some antihypertensive drugs (e.g., beta-adrenergic blockers and angiotensin-converting enzyme inhibitors).
  - Asian clients may require a smaller dose of many medications.
- Obtain a cultural history.
- Consult with someone knowledgeable about the client's cultural history and practices, but always verify beliefs with the client.
- Obtain an understanding of what the client perceives as "good health."
- Inquire about their beliefs regarding health, wellness, and illness.

The Aging Client and Pharmacology

There is an increasing number of older adults around the world. One of the terms used to describe the aging population is "silver tsunami." This somewhat negative term refers to the combination of the large number of baby boomers who are reaching retirement age, the improved life expectancy for older adults, and a reduced birth rate among younger adults. The U.S. Census Bureau projects that the nation's 65 and older age group will grow to almost 95 million individuals by 2060 (Vespa et al., 2020). This will impact the Social Security system, and there will most likely be greater demand for health care and long-term care. There is also concern that there will be a shortage of workers in many professions across the United States, including in health care.

The aging adult presents a challenge to the health care provider as health declines. As society ages, individuals have more comorbid conditions, often leading to the use of multiple medications (Pazan & Wehling, 2021). According to

the Kaiser Family Foundation (Kirzinger et al., 2019), approximately 90% of adults over the age of 65 take at least one prescription drug. They go on to report that this population also is more likely to take multiple prescriptions. Although drugs can alleviate or even cure many diseases, these same drugs can cause many drug-related problems. The nurse must be aware of these potential drug-related problems when caring for the older client.

Older adults have changes in organ function that affect their response to most drugs, from the standpoint of both pharmacokinetics and pharmacodynamics. These changes can result in an increase in sensitivity to drugs due to declining liver and kidney function. Diminished kidney function may impact the individual's ability to filter and excrete the drug. A drug's absorption rate may also be affected because transit time through the gut usually slows with age. Gastric acidity also decreases, which may impact absorption because some drugs require high acidity to dissolve. If the individual has diminished liver function, that may affect the metabolism of some medications, which may prolong the drug's effects and lead to toxicity.

Often older adults are excluded from clinical trials, just as pregnant people and children have been. When compounded by the fact that many older adults regularly take multiple medications, it can have a detrimental effect on the client. Adverse drug reactions occur more frequently in the older population and frequently cause hospital admissions and readmissions. Some of the factors that cause this increase are polypharmacy (taking many drugs), treatment with drugs that have a narrow safety margin, and multiple chronic conditions. The American Geriatrics Society (AGS) publishes a reference list of drugs called the Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults (https://openstax.org/r/geriatricscareonline).

The following are some of the pharmacologic considerations when providing nursing care for an older adult:

- Take a complete drug history at each encounter, including how the drug was prescribed.
  - Verify that the client is taking the medication as prescribed.
- Ask about new prescriptions from other providers.
- Assess the older adult's age-related sensory issues (mental awareness, hearing or visual acuity).
- Ask about any history of liver or kidney problems.
- Encourage the client to use aids such as a pillbox, especially if taking multiple drugs.
- Check the drugs for potential interactions, especially if the client sees multiple providers.
- Monitor for both expected therapeutic effects and potential adverse effects.
- Ensure the client understands the purpose of each drug, expected effects, and potential adverse effects.
- Review the drug list to determine if any drugs could be discontinued.
- Identify any potentially inappropriate drugs (e.g., drugs that cause sedation may cause a client to fall).
- Question the client about drugs they may be crushing or cutting in half. (Some capsules and extended-release pills should remain intact.)
- Encourage clients to dispose of old or expired medications.
- Determine whether the client can afford the drugs (especially new prescriptions).
- Encourage the health care provider to order the least complicated drug regimen possible.

Chapter Summary

This chapter provided a brief history of pharmacology and the use of therapeutic drugs throughout the millennia. It discussed the importance of interprofessional collaboration and introduced how pharmacology is used in nursing practice. It also presented some of the responsibilities of the clinical nurse relating to drug administration.

This chapter reviewed the many sources and forms of drugs and explained the approval process for new drugs as they come onto the market. It described the difference between the various names of the drugs (chemical, generic, and brand names) and discussed the difference between generic and brand-name drugs. Traditional drugs, biologics, biosimilars, and complementary and alternative medicine were also discussed, and counterfeit drugs, drug classifications, and drug prototypes were introduced. The various drug schedules as they relate to drugs with the potential for abuse were explained. This chapter also focused on socioeconomic factors as they relate to pharmacology and how drug therapy may impact specific groups of clients (e.g., those who are pregnant, the very young, or the very old). The chapter ended with a discussion of the aging client and the "silver tsunami."

Key Terms

adverse drug event when an individual is harmed by a drug

adverse effect an effect of a drug that is undesired

biologic a drug isolated from natural resources and developed through biomolecular science, immunology, and genetic engineering and produced through biotechnological processes

biosimilar a drug that is synthetically produced and has similar properties to a specific biologic; although it does go through testing, it does not go through the same rigorous testing that a biologic does

brand name the unique identifier of a drug assigned by the drug company and marketed to consumers; also known as a trade name

chemical name a method for identifying drugs built around the drug's specific chemical structure or composition; often of most use to the chemist or pharmacist

complementary and alternative medicine (CAM) alternative medicine refers to using a treatment instead of mainstream conventional medicine. Complementary therapy refers to using both alternative and conventional medicine together. Treatments may include massage, acupuncture, acupressure, mind–body interventions, herbs, vitamins, or dietary supplements.

counterfeit drug a product that is illegally manufactured or mislabeled regarding the identity or source and appears to be a genuine product; may be harmful to the client

drug a chemical that exerts an effect on the living body; a compound used in the prevention, treatment, diagnosis, or cure of a condition or disease

drug formulary the list of prescription drugs that are covered by an insurance plan or carried by a medical institution

drug prototype use of one drug within a class to represent all other drugs within the class—a "class representative"

enteral administration the administration of medications into the gastrointestinal (GI) tract

generic name the name of a drug, usually derived from the chemical name, that uniquely identifies the drug

intramuscular injection the administration of medication into the muscle of a client (usually deltoid or ventrogluteal in an adult and the vastus lateralis in an infant under age 2)

intravenous the administration of a medication directly into the bloodstream through a vein

over-the-counter (OTC) drug a drug or medication available without prescription

parenteral administration the administration of medication elsewhere besides the enteral (GI) route

percutaneous administration the application of drugs to the skin or mucous membranes

pharmacogenetics the study of the body's hereditary response to drugs

pharmacokinetics the movement of a drug through the body, or "what the body does to the drug"

pharmacologic classification refers to how a group of drugs can be organized by how they work in the body—the mechanism of action

pharmacology the study of medicines (or drugs) or the study of the biological effects of chemicals on the body

side effect an effect of a drug that is undesired

subcutaneous injection the administration of a medication into adipose tissue

synthetic drug a chemical compound produced in a laboratory by a drug manufacturer or illegally by individuals for illicit purposes

teratogenic harmful to a fetus by causing severe malformations or death

therapeutic classification refers to how a group of drugs can be organized by the diagnosis or disease being treated

therapeutic effects the effects that are expected and desired from a particular medication

Review Questions

1. The parent of a school-age client asks the nurse, "What is the difference between acetaminophen and Tylenol? Acetaminophen is much cheaper than Tylenol at the pharmacy. Your instructions state that my child should take 160 mg of Tylenol every 6 hours for fever if needed." What is the nurse's *best* response?
   a. "Tylenol and acetaminophen are two different drugs with similar effects."
   b. "Tylenol is a prescription medication, and acetaminophen is over-the-counter."
   c. "Please speak with the health care provider about their preference."
   d. "Since Tylenol and acetaminophen have the same active ingredients, either one is acceptable."

2. A client admitted to the emergency department reports abuse of hydrocodone and oxycodone. To which schedule do these drugs belong?
   a. Schedule I
   b. Schedule II
   c. Schedule IV
   d. Schedule V

3. A client receives a prescription for ibuprofen and wants to know if they can take Motrin instead. Which response should the nurse give the client?
   a. "Yes, Motrin is the chemical name for ibuprofen."
   b. "Yes, Motrin is the trade name for ibuprofen."
   c. "Yes, ibuprofen is the brand name for Motrin."
   d. "Yes, ibuprofen is the chemical name for Motrin."

4. The nurse is providing discharge instructions about a client's home medications. What response should the nurse give when the client asks about the difference between buying generic versus brand-name drugs?
   a. "Generic drugs have the same active ingredients as brand-name drugs."
   b. "Generic drugs undergo more rigorous testing than brand-name drugs."
   c. "Generic drugs are often more expensive than brand-name drugs."
   d. "Generic drugs are the same as over-the-counter drugs. They are not prescription drugs."

5. The nurse is preparing to administer a new medication to an older client. The nurse recognizes that drug absorption may be affected by which physiologic factor of aging?
   a. Increased enzymatic function
   b. Increased liver function
   c. Increased filtration of the kidneys
   d. Decreased gastrointestinal motility

6. The nurse is caring for a 93-year-old client weighing 92 pounds. What is the nurse's *priority* concern when monitoring for adverse drug effects in this client?
   a. Diarrhea
   b. Constipation
   c. Toxicity
   d. Decreased absorption

7. The nurse is teaching a group of nursing students about the importance of interprofessional (IP) collaboration. What is an advantage of IP teamwork?
   a. Decreased need for research into the client's disease process and treatment
   b. Improved client safety due to the use of each discipline's area of expertise

c. Increased cost of hospitalization due to the number of hospital workers involved
d. Decreased responsibility because other team members are assisting with coordinating care

8. The nurse understands that a particular regulatory agency is responsible for ensuring that drugs are safe and effective. What is its name?
a. Food and Drug Administration (FDA)
b. Drug Enforcement Agency (DEA)
c. Centers for Disease Control and Prevention (CDC)
d. Institute for Safe Medication Practices (ISMP)

9. A nurse is involved in a study incorporating small numbers of volunteers with the disease the drug is designed to treat. In which phase of an investigational drug study is the nurse involved?
a. Phase I
b. Phase II
c. Phase III
d. Phase IV

10. A 79-year-old client with hypertension has been prescribed a medication to lower blood pressure. Which action should the nurse take *first*?
a. Ensure the client understands the purpose of each drug, expected effects, and potential adverse effects.
b. Take a complete drug history and verify compliance.
c. Check the drugs for potential interactions because the client sees multiple providers.
d. Inform the client of potential resources to assist them in remembering their medications.

CHAPTER 2
Drug Administration

FIGURE 2.1 Pharmacology is the study of the biological effects of drugs on the body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION This chapter will describe the process of drug administration and the integration of the nursing process (assessment, diagnosis, planning, implementation, and evaluation) in relation to it. Client teaching as it correlates to drug administration will be discussed. To best understand what happens when the nurse administers a drug, the processes of pharmacokinetics and pharmacodynamics are explained. This chapter will also describe the different routes of administration, nursing interventions related to drug administration, and the steps of nursing clinical judgment. The chapter finishes with a discussion of the systems of measurements with conversion factors, how to interpret drug labels, and the various methods for dosage calculations.

2.1 Drug Administration and the Nursing Process

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 2.1.1 Define the steps in the nursing process and how they relate to drug administration.
- 2.1.2 Apply the steps of nursing clinical judgment to drug administration.
- 2.1.3 Examine the principles of drug administration.
- 2.1.4 Identify the “seven rights” of drug administration.
- 2.1.5 Explain the nurse’s role in client education in regard to drug administration.

This section will describe the importance of making sound decisions, developing problem-solving skills through clinical reasoning, and how the nursing process relates to drug administration. This section will also discuss the

seven rights of medication administration and the clinical judgment required for safe administration. The nursing process is a client-centered process and focuses on outcomes through a partnership relationship with the client and other health care providers.

Nursing Process

The nursing process is a method of critical thinking consisting of five steps that occur continuously while the client is in the nurse's care. (The client may be an individual, a family, a group, or a community.) It is purposeful and systematic in its progression, designed to achieve optimal client outcomes. It is a framework for the nurse to apply scientific reasoning to client care. The steps to the nursing process are linear but overlap each other in their progression:

1. Assessment of the client
2. Diagnosis of actual or potential problems
3. Planning nursing interventions
4. Implementation of nursing interventions
5. Evaluation of outcomes of nursing interventions as they relate to achieving the client's goals

The client (not the nurse) is at the center of the nursing process, which encompasses health, wellness, and illness in a holistic sense, incorporating all aspects of the client—physical, psychological, social, emotional, cultural, and spiritual. The nurse is uniquely positioned to assess the whole client, administer therapies (including medications), evaluate their effectiveness, and teach the client about how to maintain optimal wellness. The following discussion will focus on the nursing process as it relates to the administration of medications.

Assessment

Assessment is the process of data collection using a systematic method for collecting information and recognizing various clues as they relate to the client's status. Assessment should relate to both actual and potential health problems. All other steps in the nursing process are based on an accurate assessment. This information can be obtained from a physical assessment of the client, a health record review, or a health history from other providers, the client, or family members. Before administering any medications to a client, it is important to be thorough in assessing the client to prevent harm and deliver optimal care.

Present Illness and Chief Complaint

The nurse must understand why the client is under their care, the medical diagnosis, and the presenting and current symptoms that the client is experiencing. What is the aim of treatment? Medications can affect disease processes and symptoms, and the disease process may affect the medications. Disease processes such as liver or kidney failure can affect the way drugs are metabolized and excreted. At times, dosage adjustments may need to be made due to these problems. It is essential to know how the medications will work to improve symptoms (or how they could worsen them).

Current Medications, Substance Use, and Allergies

The nurse should assess the client's medication regime. Start by reviewing a list of the client's current drugs. If possible, encourage the client or family member to bring the actual medications. This includes prescription drugs, over-the-counter (OTC) medications, herbal supplements, illicit drugs, alcohol, nicotine, and caffeine. The nurse should ask specific questions. Some clients do not consider OTC drugs or herbal supplements to be important, but they do have the potential to interact with prescription medications. For example, the OTC drug ibuprofen can interact with certain medications for high blood pressure, causing the antihypertensive drugs to be less effective. Assessment of illicit drugs and alcohol use is also important. Alcohol may interact with benzodiazepines or opioids, causing respiratory and central nervous system depression. A client who recently used a street drug such as heroin, cocaine, or ketamine may also be at risk for dysrhythmias or respiratory depression. Unfortunately, these drugs may be laced with fentanyl, causing a client to be at risk for severe respiratory depression.

No medication should be given without first asking the client about allergies and reactions to medications. If a client has been previously exposed to a drug and had a mild reaction, the reaction could be more severe when they are exposed again. Some clients may reveal a reaction that is not an allergy but, instead, the result of a side effect. An example of this is a client who reports that they have an allergic reaction to diphenhydramine (Benadryl) that causes them to be very drowsy. This is a common and expected effect of this drug rather than an allergy. Once the nurse

obtains the information about both the allergy and the reaction(s), it is important to document this clearly in the client record for future providers.

Past Medical History

Similar to ascertaining a client's present symptoms and medical diagnoses, the past medical history is also important because it may impact the client's current condition and response to medications. For example, liver and kidney dysfunction may affect the way drugs are metabolized and excreted. Some drugs may be contraindicated in some chronic diseases such as diabetes, hypertension, heart failure, or chronic obstructive pulmonary disease. Is the client visually challenged, or do they lack manual dexterity? A visually impaired client with diabetes, for example, will have challenges in drawing up and administering insulin that another client with healthy vision will not. A client with Parkinson's disease or one who has had a stroke may also have difficulty with these psychomotor skills.

Psychosocial Factors

The use of alcohol, tobacco, or street drugs may affect the body's response to some medications, so obtaining a psychosocial assessment is helpful. It is also important for the nurse to know the support systems in place for the client. Are there family members or friends who are able to assist with the medications at home? Does the client have insurance? Is the client able to afford the medications? For some individuals, even paying $4 for a prescription is difficult. There are prescription drug programs that may be able to assist, and collaborating with the pharmacist or a social worker may help the client adhere to the medication regimen. A pharmacist may also be able to suggest alternative therapies that might be cheaper for the client.

Health Literacy and Education

Another important piece of this assessment is evaluating an individual's health literacy and determining a client's understanding of their disease process and the recommended treatment (including medications). **Health literacy** is a general term used to describe an individual's ability to obtain, understand, and make appropriate decisions based on information to promote their health and wellness (Taylor et al., 2023). A client who is new to their disease process may require more explanation than someone who has managed a chronic disease for years. It is crucial for a client to know why a drug is important to their health and well-being so that they will adhere to a medication regimen. It is also vital that the client understands both the therapeutic effects and side effects of the drug. Once side effects are discussed, the nurse must explain which side effects are not harmful and when to notify the health care provider of problems. Assessing the client's level of education is helpful in presenting the information in a way that will be most easily understood by the client and family.

Physical Findings and Laboratory Values

When administering medications, the nurse should complete a focused assessment as it relates to the medication to be given. For example, if giving a medication to lower blood pressure, blood pressure should be assessed before giving the drug. If that specific drug lowers blood pressure and heart rate, then both should be measured before giving the medication.

Laboratory values should also be assessed prior to giving medication. One diuretic may cause potassium to be excreted from the body, requiring the nurse to withhold the diuretic if the client is hypokalemic, but another may cause potassium to be conserved and should not be given to a client who is already hyperkalemic. Some drugs should not be given if liver enzymes are elevated; others should not be given if the kidney values of blood urea nitrogen (BUN) and creatine are elevated.

Weight and Age

A client's weight should be obtained prior to administering some drugs, especially in the pediatric population. An accurate weight will assist the nurse in determining if the dosage is appropriate.

Children and older adults may require medication dosage adjustments due to issues such as kidney or liver function changes. A child may be unable to metabolize some medications well due to an immature hepatic system or to excrete drugs through an immature renal system; however, the older adult may have a decline in kidney and liver function due to age and chronic disease conditions. Medication delivery may also need to be altered in these age groups. For example, an infant or child may need a liquid dosage form because they may be unable to swallow tablets or capsules; older adults with Alzheimer's disease or stroke may also be unable to swallow those medication forms.

Nursing Diagnosis and Problem List

In the diagnosis phase of the nursing process, the nurse uses the information from the assessment to identify and prioritize problems. Whereas the health care provider's medical diagnosis focuses on disease process or pathophysiology, the nursing diagnosis focuses holistically on any physical, psychosocial, sociocultural, or spiritual changes or problems in the client's health, wellness, or illness. Part of the assessment the nurse completes before drug administration is determining if the drug is appropriate for the client (right diagnosis or **indication**) and identifying any potential problems that might arise if the drug is given (adverse effects). Will the proposed treatment be safe and effective? In the case of the client taking an antihypertensive drug, for example, what are the potential adverse effects of the drug? Will the drug lower the blood pressure to an unsafe level? What is the client's ability to adhere to the medication regimen at home?

When considering these questions, it is important to analyze what is known about the client—the medical diagnosis; whether or not the client has taken the drug in the past; potential adverse reactions, contraindications, and allergies; comorbidities that might affect the response to the drug; potential drug–drug interactions; and current laboratory data. There are many potential nursing diagnoses or health problems related to drug administration. Consider utilizing the North American Nursing Diagnosis Association (NANDA) (https://openstax.org/r/nanda) website for more information regarding nursing diagnoses and problems.

Planning

Once the nurse has completed the assessment and has identified the actual or potential nursing diagnoses or problems, they must develop the plan. This is done by formulating client goals that address the client's problems (or nursing diagnoses) that have been identified. When possible, the client, family, and nurse should work together in the planning process to better understand the desired outcomes. Goals are written in such a way that it is clear what type of observable response should be seen (Callahan, 2023). Part of this process is prioritizing the information that was gathered in the assessment, integrating this into the nursing diagnosis, and then setting the goals with the client. Collaboration with the client and family also allows the nurse to become aware of unidentified problems that might prevent the outcome from being realized.

Consider the client with severe postoperative pain (problem) secondary to a recent right knee replacement (etiology of the problem) who has an order for an opioid agent. The goal is defined as the result that the nurse and client wish to see due to the nursing interventions (Callahan, 2023). A potential goal for the hospitalized client with postoperative knee pain could read, "The client will rate their knee pain as 4 or less on a 0 to 10 scale during this shift." Remember to include the client in this process. Is a pain level of 4 or less acceptable to the client?

The planned interventions are developed specific to the goal and are explicit actions that relate to that goal. In the previous example, the interventions might read like this:

- Assess the pain level every hour using the pain scale of 0 to 10.
- Administer hydrocodone 5/325 mg 30 minutes prior to physical therapy and every 6 hours PRN as ordered. (PRN stands for *pro re nata*, a Latin term meaning "as the circumstances arise." This medication is not a scheduled drug; it will be taken as needed.)
- Apply ice packs to the right knee for 20 minutes four to six times each day.
- Demonstrate the use of a walker to assist the client with ambulation.

It is important for goals and interventions to be client-centered and very specific. Be sure that the interventions are related to the individual goal and are realistic for the client.

Implementation of Nursing Interventions

The fourth phase of the nursing process is the implementation phase. During this phase, the interventions are performed in order to reach the client's goal(s). At the heart of the implementation phase is the concern for client safety. No goal or intervention should be planned without consideration of the client's safety in the nursing process. The nurse should assess for any potential complications during this process. Interventions or goals may need to be modified depending on the client's circumstances. In the example of the client with postoperative pain following a right knee replacement, the nurse evaluates the client's pain before a physical therapy visit. If it is not time for the pain medication to be given, it is possible that the physical therapy visit will need to be postponed.

Some potential interventions related to medication administration for this client might include:

- Assess safety prior to administering the medication (check vital signs and laboratory values). (See Appendix B: Common Abbreviations and Lab Values for typical lab values.)
- Verify the rights to medication administration (right client, right medication, right indication, right dosage range and rate of administration [if appropriate], right route, right time, and right documentation).
- Verify allergies and reactions.
- Assess for adverse effects of the medication (both before, if the drug was administered previously, and after).
- Teach the client about the medication, indications, expected effects, and potential side effects. The nurse should also explain the drug names (brand and generic), dose, route, and frequency.
- Document medication administration and any pertinent data related to that.

Evaluation

This phase of the nursing process assesses and evaluates the *outcomes* of the nursing goals and interventions. For example, has the client's pain been controlled during this shift? Did the client rate the pain as 4 or less on the pain scale? Did the client have any adverse reactions to the medication? This ongoing process evaluates the client's response to the drug—for the therapeutic effect, the development of adverse effects, and teaching needs—and anticipates discharge needs. **Therapeutic effectiveness** refers to whether the drug did what it was supposed to do. Did the pain medication relieve the pain? One intervention may assist the client in meeting the goal, but another intervention does not. In this case, the intervention may need to be modified. For example, in the case of the postoperative client who had a knee operation, if the client had developed a rash following the last dose of hydrocodone, the nurse must notify the provider to order an alternative drug to control the pain. Alternatively, if the client's pain remained an 8 on a 0 to 10 scale even after hydrocodone, the nurse will notify the provider to order an alternative drug to meet the goal of a pain level of less than 4.

The evaluation phase of the nursing process is ongoing until the client outcomes are met or the client reaches an optimal state of well-being. The client's goals and interventions may need to be modified according to the ever-changing status of the client.

Nursing Clinical Judgment

The National Council of State Boards of Nursing (NCSBN) has "developed the NCSBN Clinical Judgment Measurement Model (NCJMM) as a framework for the valid measurement of clinical judgment and decision making within the context of a standardized, high-stakes examination" (NCSBN, 2023, para. 1). Nursing students across the United States are now being tested using the Next Generation National Council Licensure Examination (NGN) model, which was first administered in April 2023. This exam helps to protect the public and measures the minimum competence of a new graduate in regard to safety. Why is this information presented in this text? The nurse must be able to problem-solve and critically think, and the clinical judgment model was developed as a way to test clinical judgment in nursing. Much of a nurse's clinical judgment revolves around medications and whether a drug is safe to give or recognizing problems.

Clinical judgment is defined by the NCSBN as "the observed outcome of critical thinking and decision making. It is an iterative process that uses nursing knowledge to observe and assess presenting situations, identify a prioritized client concern, and generate the best possible evidence-based solutions in order to deliver safe client care" (NCSBN, 2018). An iterative process is one that builds, refines, and improves the process for the best possible outcome.

Safe, efficient care of the client and improved clinical outcomes rely on sound decision-making, clinical reasoning, and clinical nursing judgment. Errors in clinical decision-making often lead to poor outcomes (Nibbelink & Brewer, 2018). According to Sherrill (2020), there are two common errors that novice nurses make that cause them to undergo disciplinary action against their license—a failure to notice and a failure to act. Failure to notice refers to failure on the part of the nurse to see a change in the condition or status of the client. Once a change in the client is observed, it is the nurse's duty to act in some way to prevent a negative outcome for the client.

The nurse must possess many skills to take care of the client: interpersonal, cognitive, technical, and ethical/legal knowledge (Taylor et al., 2023). The nurse needs to have the technical skill to administer an intravenous push (IVP) medication and subsequently document it in the electronic medical record (eMAR) as well as the ability to determine cognitively that the medication is safe to give. Interpersonal skills are necessary for the interaction between the nurse and the client during the administration of the medication or with the pharmacist and provider

when discussing potential problems that might arise from an adverse drug event. Ethical and legal responsibilities are a part of the nurse's workday each time they chart or encounter an ethical dilemma when deliberating over the risk versus the benefit of a drug. Often this can be seen in the nurse's role of advocate for the client.

Critical thinking is an essential piece of the nurse's clinical judgment and is absolutely crucial to the process of administering medications safely. The nurse must think through every decision and action before administering a drug. According to the NCJMM, the nurse must first recognize cues (Dickison et al., 2019). Where is the client located, and how do they present? For example, the client may have presented to a health care clinic in mild distress due to a cough and sinus congestion, or they may have presented to the emergency department with severe shortness of breath and chest pain. What is their history? The nurse should recognize the various signs and symptoms of a disease process and recognize abnormal vital signs and laboratory work, then hypothesize what may be occurring with the client. What is the most important thing for the nurse to assess? Analyzing the cues is important. What is the priority in this situation? How acute are the symptoms? Does immediate action need to occur? The nurse needs to have the underlying knowledge to recognize relationships between signs and symptoms and potential disease processes and likely treatments (including medications). However, the ability to recall nursing knowledge is only part of the nurse's thinking; the nurse then needs to make the clinical judgments suitable to the situation (Silvestri et al., 2023). What interventions will be most helpful in this situation? Once the nurse intervenes, the question then becomes whether those actions and decisions helped the client.

The nursing process is an integral piece of nursing clinical judgment and embraces the critical thinking process. The nursing process was discussed earlier in this chapter in relation to medication administration. The nursing process can be integrated into the clinical judgment model.

Recognizing cues is the nurse's skill of observing cues or signs and symptoms of a client's problem (Dickison et al., 2019). This is accomplished through assessing (the first part of the nursing process). A nurse collects information from many different resources. An example of this might be the nurse who is caring for a client who experienced a myocardial infarction 3 days ago and is to administer metoprolol, a medication that decreases blood pressure and heart rate. The nurse recognizes that those parameters should be assessed prior to giving the drug. Other data will be collected that the nurse then needs to sort through and determine which information is expected and which is unexpected or concerning. The nurse should assess and recognize that the blood pressure of 84/60 mm Hg and the heart rate of 48 beats per minute with the symptoms of dizziness are abnormal.

Analyzing cues is the skill of organizing the information obtained and linking it to the situation (Dickison et al., 2019). Continuing with the previous example, the nurse interprets the data and recognizes that the blood pressure and heart rate are too low to give the metoprolol. A nursing diagnosis or problem list can be formed during this phase based on the assessment data. The nurse requires a knowledge of the pathophysiology of myocardial infarction and knowledge of the therapeutic and adverse effects of metoprolol. The clinical reasoning model uses critical thinking to understand that the nurse recognizes the problem and knows what to do in response to the findings.

The next phase of the process is to *prioritize hypotheses* (Dickison et al., 2019). This means the nurse will attempt to focus on the meaning of the information that has been obtained and prioritize the client's problems (Silvestri et al., 2023). What is the priority problem for the client on metoprolol mentioned above? In this example, the client has three problems:

1. Low blood pressure, which may be due to the myocardial infarction or a previous dose of metoprolol
2. Low heart rate due to a previous dose of metoprolol
3. Dizziness due to the abnormal blood pressure and heart rate

The next phase of the process is to *generate solutions* (Dickison et al., 2019). In this phase, the nurse wants to consider all possible actions that might be utilized to resolve the problem(s). Many times, this includes actions that will be implemented to achieve the desired outcome, but sometimes this will include withholding a medication or recognizing which actions should be avoided (Silvestri et al., 2023). In this instance, the nurse may predict complications of further lowering of the blood pressure and heart rate if the metoprolol is administered. The consequences of administering metoprolol to the client might mean a critical drop in the blood pressure or heart rate, potentially even causing shock.

Dickison et al. (2019) then state that the next phase of this model is *taking action*. In the example given, the actions

the nurse takes during this phase are to withhold the medication, metoprolol, and notify the provider of the problem. This aligns with the implementation phase of the nursing process.

Evaluating outcomes is the last clinical judgment thinking skill in the clinical reasoning model and aligns with evaluating the interventions that the nurse implemented (Silvestri et al., 2023). The nurse must evaluate the outcome of whether the client meets the goal of improved blood pressure and heart rate when the metoprolol is withheld.

These processes are not linear; they are cyclical. The nurse will continue to assess, recognize, analyze, generate solutions, respond by taking action, and reflect on the outcomes. The nurse expects the outcome of the blood pressure and heart rate to return to baseline after holding the metoprolol; however, the nurse must continue to reassess the client to ensure that this occurs and act accordingly. If the blood pressure and/or heart rate do not increase, the nurse must then implement other interventions and evaluate whether they were successful.

This example of clinical judgment actually occurs before administering the drug. A similar process would occur even if the blood pressure and heart rate were normal. Then the process would occur again when the nurse assesses the client for adverse effects.

Principles of Safe Drug Administration

Safety is a fundamental element in the process of medication administration. It is important to demonstrate good clinical decision-making skills throughout the procedure. The focus of the nurse's clinical judgment during medication administration begins with first knowing the client and assessing the relevant information according to the medications that need to be delivered. **Medication reconciliation** is performed to ensure that the medications that the provider has ordered are accurate and appropriate for the client. Medication reconciliation is the process of identifying and verifying the most accurate list of medications that a client is taking. This should include the drug name, dosage, frequency, and route for the client. This process should also determine why the client is taking the medication. It should include all over-the-counter medications, vitamins, and supplements. This list is then compared to the provider(s) list. This process should occur at any transition in care (admission, transfer to another unit, discharge, and clinic visit). The nurse should scrutinize the list for duplications, incorrect dosages, and omissions (Agency for Healthcare Research and Quality [AHRQ], 2019). Once a focused physical assessment and laboratory assessment have been completed, the client should be informed about the drugs that have been prescribed. If the nurse is unfamiliar with a drug, it is crucial that they learn about it before administering it. Many resources are available to the nurse for that purpose—drug guides, the pharmacist, drug insert labels, or drug apps on the phone or computer, to name a few.

When planning drug administration, the nurse needs to keep safety foremost in mind. Medication errors are common, preventable errors with far-reaching consequences for the client, the institution, and the nurse. The U.S. Food and Drug Administration (FDA) receives more than 100,000 reports of potential drug errors each year (not all errors are reported to the FDA) (FDA, 2019). Tariq et al. (2023) reported that the cost of caring for individuals who had been the victim of drug errors is over $40 billion each year. A meta-analysis by Panagioti (2019) reported that 1 out of 20 clients may be impacted by a preventable medical error and that as much as 12% of this preventable harm results in death or disability. Of these errors, medication-related errors accounted for the majority. Ethics, Legal Considerations, and Safety discusses medication safety in further depth and emphasizes additional strategies to prevent errors.

Medication safety means ensuring that the right dosage of the right drug is administered to the right client at the right time by the right route or the right reason, and it is documented correctly (the seven rights of medication administration; see Figure 2.2). Nursing practice has expanded the original five rights of medication administration to seven. These rights have been identified as basic standards of care in medication administration in order to preserve client safety. Most institutions require nurses to review these rights at least three times before administering medications. An example of what can happen if all seven rights are not followed might look like this: the nurse has the right dose of the right drug via the right route at the right time for the right reason, but if the nurse walks into the wrong room and fails to identify the right client, a medication error (and potential harm) occurs.

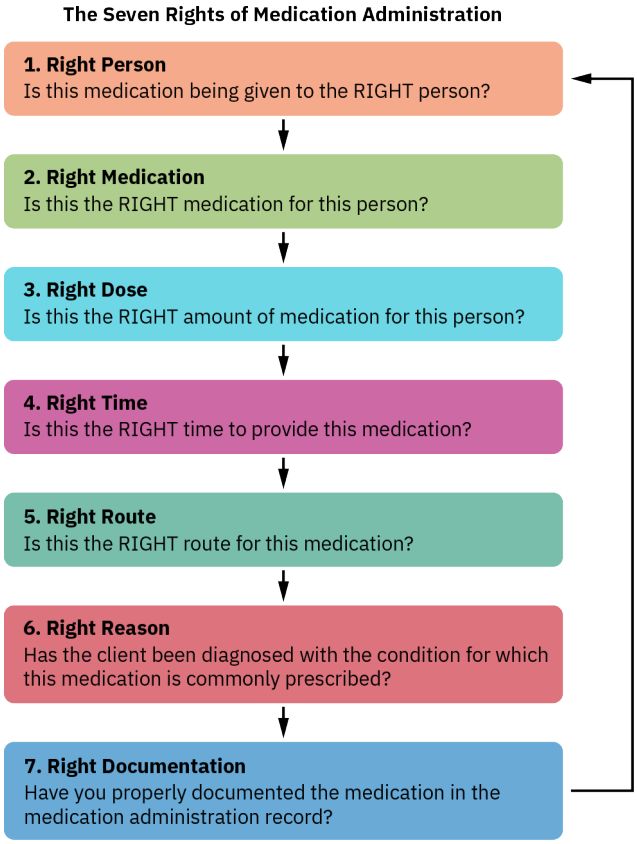


FIGURE 2.2 Adhering to the seven rights of medication administration will help the nurse administer drugs safely. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The seven rights are:

- *Right client (person):* The Joint Commission recommends using at least two identifiers to ensure that the nurse administers drugs to the right client. Name, date of birth, and/or medical record number are standard client identification methods. Confirming two identifiers safeguards the client from harm. When possible, request that the client verbalize their name and date of birth while verifying this information by comparing it to the wrist ID band and the client's chart.
- *Right medication:* Most institutions have policies in place to ensure that the right client receives the right medication. Medication dispensing systems and barcode scanning are additional processes that many institutions use to assist the nurse during administration. The nurse must compare the medication label or container three separate times—once when obtaining the medication, again when preparing the medication, and finally, and most importantly, when at the bedside. The nurse should also check the expiration date and verify that the medication was stored properly. The nurse should know the action of the medication and how it is to be administered so that all materials can be obtained when drawing up the drug. Allergies and reactions should also be verified to prevent a client from getting a drug to which they are allergic.
    - *Barcode scanning:* For institutions that use barcode scanning, each drug container (usually a unit dose package such as a blister pack, vial, or prefilled syringe) is labeled with a unique barcode. The information in the barcode allows for the comparison of the medication being administered with what the health care provider ordered for the client before administration. The nurse first signs into the computer or uses the barcode scanner, a handheld device, to scan the barcode on the clinician's badge. The nurse then uses the scanner to scan the barcode on the client's unique client identification wristband and the drug. The system then verifies the drug to be given with the order in the system. The clinician is given a warning if the information does not match. Strudwick et al. (2018) report in an integrative review that barcode technology significantly decreases medication errors when proper scanning is completed consistently *before* administration.
- *Right dose:* The nurse must validate the right dose and any drug calculations that were performed. They can

ask another nurse to validate doses of high-alert (more dangerous) drugs, such as heparin or insulin. The nurse needs to know the usual safe dosage ranges and maximum doses to ensure safe administration and question doses that are outside the usual range or seem unsafe.

- *Right time:* Each institution has its own policy regarding acceptable time frames for medication administration. Most institutions allow a drug to be given within a time frame of 30–60 minutes before or after the scheduled dose. Drug schedules are important to keep drug concentrations steady. If a drug is given too early, this might result in a drug overdose; however, if it is given too late or omitted, then the client may be undertreated.
- *Right route:* The nurse must administer the drug via the correct route and verify that the route is safe for that particular client. They should never assume the route of administration—it must be confirmed with the provider if it was omitted from the order.
- *Right indication for use (reason):* The nurse confirms why the client has been ordered the medication; for example, beta-adrenergic blockers may be administered for angina, hypertension, myocardial infarction, dysrhythmias, or heart failure. Knowing why the medication has been ordered will assist the nurse in assessing the drug's therapeutic effect. They should clarify orders that do not seem appropriate for the client.
- *Right documentation:* The nurse needs to ensure that documentation is completed after the drug has been administered. They should not document medication administration prior to giving the drug. If there was any variance in the drug administered, the nurse needs to ensure that the reason is documented. The nurse also should document if the client refuses the drug and why, as well as if a medication was withheld and the explanation for holding it.

LINK TO LEARNING

The Seven Rights of Medication Administration

Access multimedia content (https://openstax.org/books/pharmacology/pages/2-1-drug-administration-and-the-nursing-process)

This video provides more information about the rights of medication administration in nursing. A BSN/RN explains the rights of medication administration and gives examples and anecdotes from their own experiences.

Nurses should encourage clients to participate in their care by questioning the nurse about the medications being delivered. Collaboration with other health care providers will also assist in keeping the client safe during medication administration. In the inpatient setting, the verified medications are withdrawn from the medication dispensing machine, the materials needed to administer the drugs are obtained, and all are taken to the client. The medication should remain in the original container until the nurse is at the bedside, ready to administer the medication. The nurse identifies the client, using two unique client identifiers, and the drug is reverified as the correct drug before giving to the client. The medication can be reverified by checking the drug label with the medication administration record or through the use of barcode scanning, where available, at the bedside prior to administering the medication. The nurse follows medication administration by planning on when to reevaluate the client for therapeutic response and adverse effects.

Client Education and Drug Administration

One important responsibility that a nurse has is client education. According to the American Nurses Association (2021), teaching and promoting health and wellness is expected of the nurse providing care to a client. Teaching is about using specific strategies to reinforce or change specific behaviors. Learning is the desired outcome that results from teaching. A change in behavior is the evidence of teaching and learning. The primary target for teaching in the health care setting is the client and family or caregiver. In order for the nurse to be an effective teacher, it is important to understand how individuals learn. There are three domains of learning: cognitive, psychomotor, and affective.

Cognitive Domain

The cognitive domain of learning is the *thinking* domain within the learning process. Concepts related to this domain include knowing, comprehending or understanding, applying, analyzing, evaluating, and synthesizing. Within this domain, an individual's past experiences and perceptions are important to consider because they will impact the client's ability to learn. The foundation for any learning experience is a person's previous experience and knowledge.

Teaching a client with diabetes about insulin, how it works, its therapeutic effects, dosing, and side effects is within the cognitive domain.

Psychomotor Domain

The psychomotor domain relates to *doing* or *skill*, specifically motor skills. Nurses will frequently teach clients various skills related to their disease process. The nurse who teaches the client about insulin and demonstrates how to inject themselves with a dose of insulin is teaching within the psychomotor domain. The client with diabetes learning within the psychomotor domain will need to learn the physical skill of drawing up the insulin and then injecting the insulin into their body.

Affective Domain

The affective domain refers to the *feelings, emotions, and beliefs* within the learning process. It also encompasses an individual's interests and attitudes toward learning. The client with diabetes who is frightened about shots and is anxious about this process may have difficulty learning the skill of giving injections.

Ideally, the nurse will use each domain in the teaching plan for the client. In order to be an effective teacher, the nurse will try to develop a positive teacher–learner relationship by developing different approaches for different learning styles. For a learner who learns best by doing the skill, the nurse should encourage the client to practice the skill under their supervision rather than simply explaining what must be done. It is important to assess the client's readiness for learning and adapt strategies that will help the process.

Factors that Influence Learning

According to Callahan (2023), many factors may facilitate learning in the client. The information needs to have relevance to the client. Someone who is actively involved in the learning process and is motivated to learn will usually master the content more readily. The nurse can approach the client and determine their readiness to learn. The client may wish to have a support person(s) with them to help them retain the information. The nurse should begin with a simple explanation and expand to more complex topics as time allows. Repetition is helpful in the learning process to reinforce the concepts. The nurse may make further arrangements to continue teaching or pass this on to a colleague as appropriate.

There are also many potential barriers to learning; for example, a client who is extremely anxious or in a lot of pain may not have the ability to focus on the process. Other common barriers include:

- Educational level
- Developmental level
- Attitudes, values, and beliefs
- Unmet needs
- Emotions (fear, anger, depression)
- Physical health status (pain, anxiety, medication, fatigue, hunger)
- Self-concept
- Self-esteem
- Cultural considerations (the individual's health beliefs and practices)
- Language barriers
- Lack of motivation
- Lack of readiness
- Psychomotor ability (e.g., the client with Parkinson's disease or who has had a stroke may have the cognitive ability to understand how to give an injection but may be limited physically by muscle strength or coordination)

Developing a Teaching Plan

To develop a teaching plan, the nurse should assess the client's learning needs. (The first part of the nursing process is to assess.) Determine their disease process, discover what the client already knows, and discuss the client's support system. Consider the client's characteristics. Are they motivated to learn? Are they ready to learn? What is their reading and comprehension level? What are their health and belief practices? What is their learning style? Do they learn best by visualizing material in colors, maps, and diagrams? Or do they learn best by listening (auditory learner) or by doing (kinesthetic learner)? Another characteristic to assess is the client's health literacy and where

they obtain information. According to the Agency for Healthcare Research and Quality (Bakerjian, 2023), health information should be written in plain, straightforward language and should not exceed a sixth-grade reading level. The information should use short sentences with pictures that illustrate instructions for the client. This should be adapted according to the educational level of the client. Teach the priority information first and then repeat as needed.

Part of the teaching process is to evaluate the learning. This is an ongoing process, and consideration of the evaluation tools is important. Direct observation of behaviors and asking the client to teach back information or demonstrate a skill back to the nurse are helpful ways to evaluate learning (Bakerjian, 2023). It is important to ask for feedback and clarify when information is unclear. In order to promote a helping-trust relationship, the nurse should instill faith and hope in the client while providing a supportive environment.

Teaching Resources

Discover the teaching materials at your institution. Most institutions have written materials, and some have various smart tablets or e-health portals for educational information. Information provided by institutions or health systems is considered reliable and accurate and can be very helpful to clients and their family members.

Many clients have smartphones and can access health learning applications with tutorials and quizzes that help the learning process. A great deal of information is available to the client through the internet, and the nurse can assist them in finding the appropriate websites to obtain reliable information on their disease process and treatment.

TRENDING TODAY

Determining a Website's Reliability

The National Institutes of Health (2022) provide these guidelines for determining the reliability of websites:

- Is there an author listed? If so, what are their qualifications?
- What is the website's address? (Credible websites usually end in either .gov, .org, or .edu.)
- Who pays for the website?
- Is the website current? Are there references? Are there working links?
- What is the content? Is it biased? Is it opinion? Is it fact? Why was it written?
- Is it trying to sell a product?
- How is the website constructed? Can the information be easily found?

Many applications (apps) available on phones or smartwatches can assist the client and provider in monitoring the client's health, including pulse rate and rhythm monitoring, blood pressure monitoring, and blood glucose monitoring. It is helpful to the client if the nurse has firsthand knowledge of the site or applications recommended. Using reliable, credible resources can help the client and family make more informed decisions and become an active participant in their care.

2.2 Pharmacokinetics and Pharmacodynamics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 2.2.1 Define how body cells respond to drugs.
- 2.2.2 Explain the meaning of the half-life of a drug.
- 2.2.3 List the factors that can influence the effectiveness of drugs in the body.
- 2.2.4 Differentiate between side effects and adverse effects of drugs.
- 2.2.5 Describe drug tolerance and drug toxicity.

Before administering a medication to a client, the nurse must understand what the body does to the drug and what the drug does to the body. Drugs produce effects on the body's physiology by making chemical changes that affect certain target cells within the body. The term **pharmacodynamics** essentially means "what the drug does to the body." The root word, *pharmaco,* refers to medicines, and *dynamics* means change, so it refers to how the drug changes the body. All living organisms are composed of chemicals that function through various chemical reactions. When chemicals (drugs) are added to this structure, those chemicals change the body. Essentially,

pharmacodynamics examines the relationship between drug concentrations at the drug's site(s) of action and the subsequent effects of the drug in the body—its mechanism of action.

The term **pharmacokinetics** refers to how the body processes the medicine. The word can be broken down to the root word, *pharmaco*, meaning medicines, and *kinetics*, meaning movement. Once the nurse understands pharmacokinetics, they can better understand a drug's actions, effects, interactions with other drugs, dosing frequency, and precautions. The four primary processes of pharmacokinetics are *absorption, distribution, metabolism,* and *excretion*. These will be discussed in the following sections.

Drug Absorption

Absorption refers to the process of a drug traveling from the site of administration, through the body's membranes, and into the circulating bloodstream. Drugs may be absorbed through the skin (i.e., topical medications), through the membranes in the respiratory tract (i.e., inhalers), through the membranes of the gastrointestinal tract (i.e., rectal medications and most pills, tablets, and capsules), or through subcutaneous (i.e., **subcutaneous** injections) or muscular (i.e., **intramuscular injections**) tissues. The route of administration influences the absorption of a drug. A drug's physical and chemical properties affect the absorption rate, as do the physical and chemical properties of the client's body. Absorption also affects the amount of time it takes for a drug to take effect. Some of the factors that may affect the rate of drug absorption or the extent to which a drug is absorbed include:

- *Formulation of the drug:* Liquid formulations of oral medications are absorbed more rapidly than capsules or tablets.
- *Lipid solubility:* Lipid-soluble drugs are absorbed more quickly than water-soluble ones.
- *Size of the drug's molecules:* Large molecules are less readily absorbed than smaller molecules.
- *Blood flow:* Drugs are more rapidly absorbed in areas where blood flow is high.
- *Route of administration:* IV drugs enter the bloodstream immediately; other routes take the body longer to absorb.
- *Surface area:* The larger the surface area where the drug is to be absorbed (e.g., small intestine vs. the stomach), the quicker the absorption rate.
- *Acidity:* For oral medications, the acidity of the stomach or intestine can affect absorption.
- *Gastric motility:* This may either slow down or speed up absorption, depending upon motility.
- *Coatings:* Special coatings on oral preparations can affect absorption.
- *Food:* The presence of food in the gut can affect the absorption of oral preparations.

As mentioned above, surface area can greatly affect drug absorption. This may impact both the speed of absorption and the extent to which a drug is absorbed. Drugs administered via the respiratory tract as gases or aerosols are quickly absorbed due to the large surface area of the lungs and the very rich blood supply there. The alveolar epithelium is quite permeable, which also aids in absorption. Oral medications may be absorbed in the stomach or the small intestine (sometimes both). The small intestine has many mucosal villi and microvilli, which increases its surface area; this allows medications to be more rapidly absorbed when compared to the stomach, which has a relatively small surface area. When areas of the small intestine are removed, this greatly impacts drug and nutrient absorption.

Bioavailability refers to the amount of the active drug entering the circulation and available at the site of action—or the physical ability of a drug to reach its specific target cells to have an effect on the body. Price and Patel (2022) define bioavailability "for majority purposes" as "the fraction of the active form of a drug that reaches system circulation unaltered." Typically, only a fraction of the administered dose enters the circulation unchanged, thus becoming bioavailable. For example, the antibiotic gentamicin is 0% bioavailable when taken orally because this drug is not absorbed by the small intestine; however, it is well absorbed following intramuscular (IM) administration, and it is 100% bioavailable with **intravenous** (IV) administration. IV medications are immediately 100% bioavailable because there are no barriers to absorption. Oral medications, in contrast, have several barriers to absorption, such as the pH of the stomach (acidity), the length of time the oral medication spends in the stomach, blood flow to the gastrointestinal (GI) tract, or the presence of food in the stomach. After absorption, oral drugs can also be metabolized in the liver before entering systemic circulation, a process called first-pass metabolism. This can decrease the bioavailability of a drug. Therefore, oral medications are not as readily bioavailable. First-pass effect will be explained in further detail in the section "Drug Metabolism or Biotransformation."

Drug Distribution

Drug **distribution** refers to the movement of a drug through the body or the way that a drug is spread throughout the body. There are several factors that may affect distribution:

- Blood flow or tissue perfusion
- Protein binding
- Permeability of the cell membrane
- Volume of distribution (the smaller the volume, the less distribution; the larger the volume, the more distribution)

The blood and lymphatic systems are the primary vehicles for the transport of drugs throughout the body. The most vascular organs, and the organs receiving the most blood supply, are the heart, liver, kidneys, and brain. The more vascular the area, the higher the concentration of a drug. Areas such as adipose (fatty) tissue, the skin, and bone are less vascular and more difficult to deliver high concentrations of a drug. Tissue perfusion itself can affect distribution; for example, in a client with an infected diabetic foot ulcer, it is more difficult to deliver systemic antibiotic therapy to the area to kill the bacteria because blood flow is not adequate.

Drugs are often bound to proteins in the blood to be carried into the bloodstream; however, a drug may also be considered free or unbound. Only a free drug can act at its target site of action, such as receptors, or cross into other fluid compartments within the body (Grogan & Preuss, 2022). Drugs compete for protein-binding sites within the bloodstream, primarily albumin. The more a drug is bound to a protein, the more difficult it is for the medication to be freed and able to cross cell membranes and act on the body. In order for a drug to act on a tissue, it must be released from the protein's binding site. Only the unbound portion of a drug can disperse into the tissue and interact with cell receptors to produce the intended physiological effect of the drug. According to Grogan and Preuss (2022), drug distribution aims to achieve effective drug concentration at its intended receptor site. If there is a decrease in the plasma protein binding, this increases the amount of free drug available. This will intensify the effects of the drug and may even lead to **toxicity**.

The drug must be able to cross through cell membranes to reach target sites. Medications that are lipid-soluble can rapidly cross cellular membranes because of the high permeability of capillary endothelial membranes. These drugs will be distributed more widely than those drugs that are water-soluble.

There are deterrents to the distribution of drugs. The blood–brain barrier is a protective system that prevents many drugs (and foreign invaders or poisons) from entering the central nervous system. Some drugs readily cross the blood–brain barrier, such as those that are lipid-soluble or poorly bound to proteins (e.g., sedatives, anticonvulsants, and antianxiety agents); however, many antimicrobials are ineffective against central nervous system infections because they are unable to cross the blood–brain barrier. Many antitumor drugs also fall into this category, making cancer of the brain difficult to treat with standard chemotherapy drugs.

Drug Metabolism or Biotransformation

Biotransformation or **metabolism** is the process of chemically changing a drug into a form that can be more readily eliminated from the body. This process occurs primarily in the liver by enzymes that change medications into inactive forms of the drug; however, metabolism of drugs may occur at other sites in the body, such as the lungs, vasculature, and lining of the GI tract. The enzymes for metabolism detoxify chemicals or substances to keep the body functioning at an optimal level. Sometimes these enzymes alter the drug form into an inactive metabolite, a soluble compound, or even a more potent metabolite. Cytochrome P450 (CYP) enzymes, for example, aid in the metabolism of drugs, and the liver is the primary site for CYP activity. These enzymes target primarily lipid-soluble drugs.

Drugs that enter the GI tract first go to the liver, which detoxifies and treats them using the necessary enzymes. This is known as the **first-pass effect**, and there may be variability of this effect between clients. This may affect the dosing of some medications among different clients. (See the following section for more on the first-pass effect.) It should be noted that any client with liver disease or cirrhosis can have decreased metabolic activity, making them more susceptible to dose-related side effects if they are taking a medication metabolized through the liver. Someone with cirrhosis will not metabolize a drug to the same extent as a client without liver disease, and this may lead to higher concentrations of the drug in the system. Those higher concentrations, in turn, can lead to adverse

effects. For example, the drug acetaminophen should be monitored carefully or avoided in clients with underlying liver disease. The other concern that should be mentioned is that of drug toxicity, which may occur if clients have liver disease. Clients with elevated liver enzymes may have difficulty metabolizing the drug, which may cause toxic drug levels in the client. Monitoring liver enzymes and drug-level concentrations will help ensure that drug concentrations remain therapeutic (Herman & Santos, 2023). Aspartate transaminase (AST) and alanine transaminase (ALT) are two common liver enzymes to monitor because the elevation of these enzymes may indicate hepatic dysfunction or liver damage. AST is an enzyme that assists in the metabolism of amino acids, while ALT converts proteins into energy for the liver cells.

First-Pass Effect

Any medication ingested orally is most commonly absorbed in the small intestine and transported through the portal venous system to the liver (see Figure 2.3). As the drug circulates through the liver, it is transformed by the liver enzymes into various metabolites. Some metabolites are active and will cause effects on the body, whereas others are inactivated and will be excreted from the body, largely through the stool. A *significant* part of any oral dose of a drug is destroyed through this process and will never reach its intended tissues or target cells. This is known as the first-pass effect. The active portion of the drug will then be circulated in the bloodstream and transported throughout the body to exercise its intended action. The first-pass effect can potentially decrease the bioavailability of a drug significantly. This means that an oral drug must be given in much larger doses as compared to IV administration in order to obtain similar systemic concentrations. In some circumstances, the drug cannot be given orally at all due to being completely inactivated by the first-pass effect. Instead, the drug must be given parenterally so that it can bypass this effect. The first-pass effect process is summarized as follows:

- The client ingests an oral medication.
- The drug travels from the mouth to the esophagus, the stomach, and then the small intestine.
- The medication is absorbed by the intestinal mucosa, and it travels across the membranes into the portal vein.
- Once the drug is in the portal circulation, it travels to the liver.
- During the first pass through the liver via the portal circulation, the drug is metabolized into active and inactive metabolites.
- The drug metabolites then enter the circulation and travel to target cells in various tissues where they exert their action.
- Inactive metabolites are excreted through the stool.

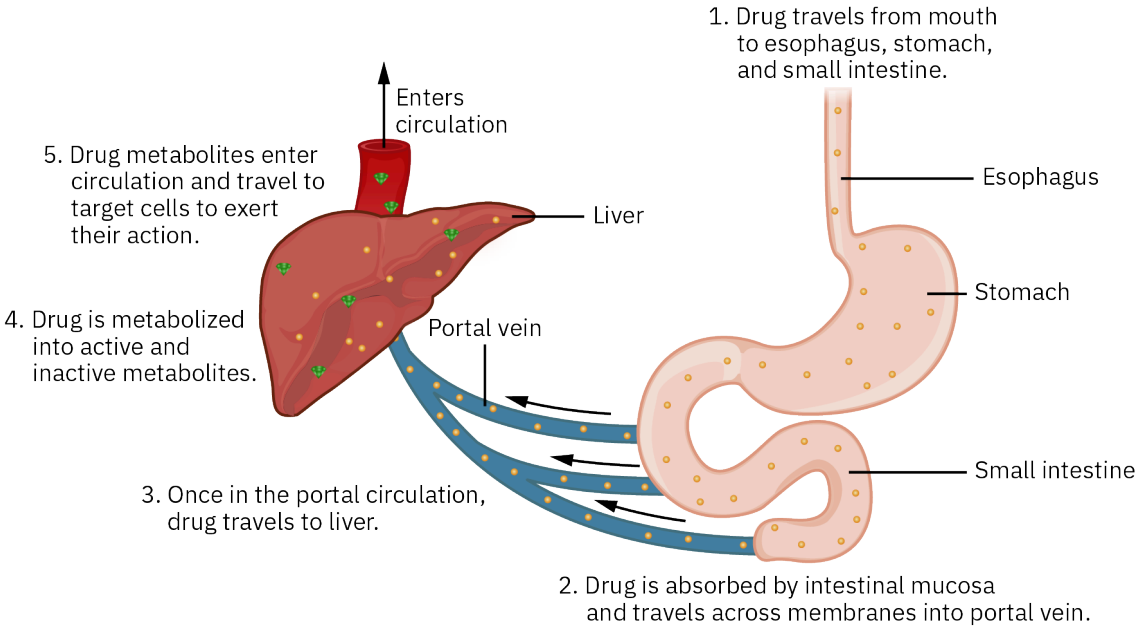


FIGURE 2.3 This figure illustrates how a drug is processed by the body in the first-pass effect. This process prepares a portion of the ingested medication for therapeutic use by the body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

LINK TO LEARNING

First-Pass Effect

Access multimedia content (https://openstax.org/books/pharmacology/pages/2-2-pharmacokinetics-and-pharmacodynamics)
This video provides a visual explanation of the first-pass effect. It concisely describes bioavailability and first-pass effect, important concepts in pharmacokinetics.

Drug Excretion

Drugs are eliminated from the body through the process of **excretion**. Although the removal of a drug occurs primarily through the renal system, it may also occur through the lungs, skin, bile, or feces. The two primary routes of excretion are the kidneys via urine and the GI tract via feces. Water-soluble drugs are readily removed from the body through glomerular filtration and eliminated in the urine. Because most drugs are metabolized in the liver and have undergone extensive biotransformation there, by the time the metabolites reach the renal system, only a small fraction of the drug remains.

There are several factors that affect the urinary elimination of drugs:

- Presence or absence of kidney disease
- Perfusion or blood flow to the kidneys
- Maturity of the kidneys
- pH of the urine
- Other drugs (e.g., NSAIDs decrease renal blood flow and alter the glomerular filtration rate [GFR])

CLINICAL TIP

Renal Function Tests

Prior to administering a medication, the nurse should always assess the renal function tests, if available. Blood urea nitrogen (BUN) and serum creatinine are two important tools to assess the kidneys. Renal disorders such as chronic kidney disease may increase a drug's action and duration, and clients will often need to have dosage adjustments to prevent toxicity. As clients age, they experience a decline in both kidney and liver function, and the nurse must be alert to the possibility that the metabolism and excretion of drugs can be affected. Drug concentrations may increase because they are not properly eliminated, leaving the client vulnerable to drug toxicity.

Half-Life

The **half-life** of a drug is the amount of time it takes for the serum concentration to reduce by 50%. For example, if a client takes a 500 mg tablet with a half-life of 4 hours, then 4 hours after administration, the amount remaining of the drug will be 250 mg. Eight hours following administration, the amount remaining will be 125 mg. (This is one-half of the previous level.) Twelve hours after administration, the amount remaining will be 62.5 mg. Half-life is important because it helps determine the dosing frequency of a medication. The half-life of medications varies widely. The antidysrhythmic medication adenosine has a half-life of less than 10 seconds, so it clears the bloodstream quite rapidly; however, another antidysrhythmic medication, amiodarone, has a half-life of roughly 100 days. It takes approximately five half-lives for the drug to be considered functionally eliminated (or 97% eliminated) from the body.

Morphine has a half-life of 3 hours. If a client were given 20 mg of morphine, in 3 hours that amount would decrease by 50% (10 mg would be gone from the body). If the client were given 2 mg of morphine, then in 3 hours, the amount would drop to 1 mg. Acetaminophen also has a half-life of 3 hours. If a 500 mg tablet is given, then in 3 hours, the amount of drug in the body will be 250 mg; however, the client given a 325 mg tablet will have approximately 162.5 mg of the drug in their body at the end of 3 hours.

Many medications must reach a threshold concentration in order to have a therapeutic effect; this is the **minimum**

effective concentration (MEC). Medications that have a short half-life leave the body quickly, in less than 8 hours, and will need to have short dosing intervals because the concentration quickly drops below the minimum effective concentration. Medications with long half-lives (greater than 24 hours) will leave the body more slowly and will be prescribed less frequently or at lower doses. Medications with longer half-lives may pose a greater risk for drug toxicity because of their propensity to accumulate in the body.

Many factors impact drug half-life, but the most significant are metabolism and excretion. Those can be affected by:

- End organ function
- Age
- Genetic factors
- Some disease processes

Drug Therapeutic Index

The **therapeutic index** refers to the range of dosing that is both safe and effective—the amount of drug that can produce a therapeutic effect but not so much that it causes a toxic effect (see Figure 2.4). Sometimes the therapeutic range is very narrow, meaning only a small amount of extra drug causes toxicity and a small decrease in the dosage may cause subtherapeutic effects. The wider the range, the safer the drug because small changes to the dose are less likely to cause toxicity. An example of this is some blood thinners or anticoagulants. They must make the blood thin enough to prevent clots from forming, but if too much is given, the client can suffer from life-threatening bleeding. Conversely, over-the-counter drugs usually have a wide safety margin, or therapeutic index. Drug monitoring is sometimes required for drugs with a narrow therapeutic window to ensure that the client's drug level stays within a safe range.

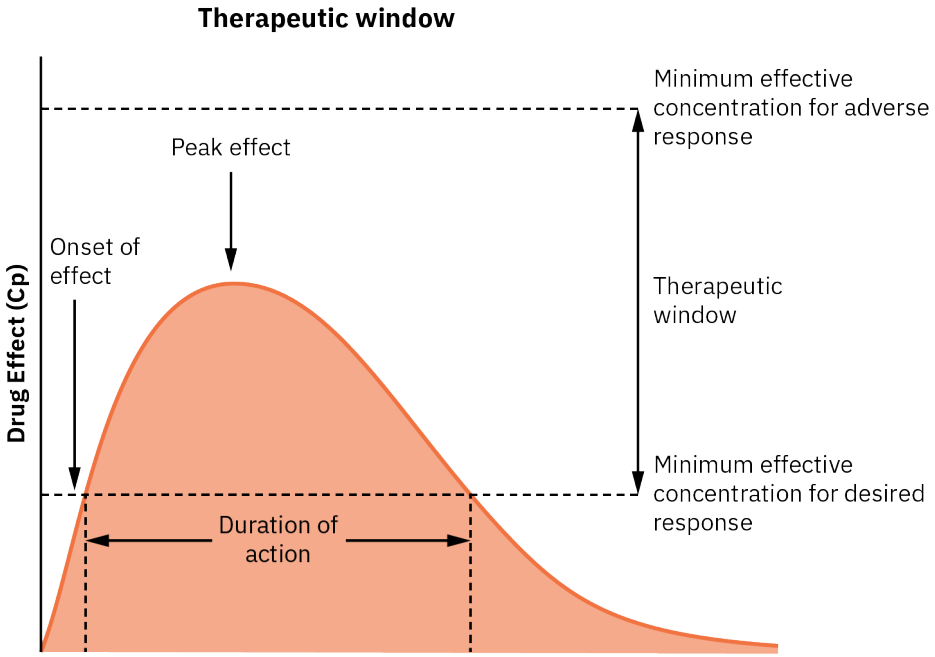


FIGURE 2.4 The therapeutic window of a medication includes the onset, peak, and duration of the medication. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Onset, Peak, and Duration of Action

A drug's therapeutic effects are usually directly related to the serum drug concentration. Most drugs work in specific target tissues; however, blood concentrations may allow providers to approximate drug concentration at the site of action. The onset, peak, and duration of action are terms that are used to describe drug effects. The **onset of action** for a medication is the time required for the drug to produce a therapeutic response (the minimum effective concentration). For example, for a drug that lowers blood pressure, it is the time between administration of the drug and onset of its hypotensive (blood pressure–lowering) effect. As the drug continues to absorb, it eventually reaches its maximal or peak level. A drug's **peak** effect describes the time required for the drug to produce its *maximum* therapeutic response. The **duration of action** is the length of time a drug produces a therapeutic response.

Receptor Response

Generally, a **receptor** is a molecule composed of a protein, found on the inside of a cell (intracellular receptor) or on the surface of a cell (cell surface receptor), that binds to specific external transmitters or messengers and causes a response in the cell. Each type of cell in the body contains unique receptors that allow the cell to react in a specific fashion in response to a set of signaling molecules. These receptors do not exist specifically to bind with drugs; in general, they naturally bind with endogenous substances such as neurotransmitters or hormones. However, due to the nature of drugs as chemical agents, they also can interact at receptor sites. The interaction between a drug and a receptor is what comprises the drug's mechanism of action or the drug's effect.

Receptors can bind with a drug and cause various beneficial pharmacological actions in different disease states. Consider the action of a receptor similar to that of a lock and key. The receptor unlocks a response to a chemical (the drug), which then affects enzyme systems within the cell (see Figure 2.5). This activated enzyme system then produces specific effects, sometimes affecting cell membrane permeability, changing cellular metabolism, or changing cellular activity. Often, a particular activity of the cell is either heightened or inhibited. Sometimes drugs will bind to a receptor site and cause an effect, whereas other times, another drug will bind to the same receptor and prevent the first drug from binding with the cell (thus blocking the effect of the first drug). This is further explained later in this section in the discussion about agonists and antagonists.

The more selective a drug is, the more ideal the drug is. This is because its selectivity for specific receptors reduces the potential side effects of the drug. If a drug is specific for only a few receptors, it limits the response to the drug—similar to a key that opens only one door. When a drug can interact with a wide variety of receptors, it can have a wide variety of responses—this would be a master key. The master key is not better than the single key—they are simply different. The single key (or receptor), however, allows for fewer side effects.

With the advent of the Human Genome Project, scientists have discovered that drug therapy is not an "one-size-fits-all" therapy. Some individuals may have fewer receptors than others, whereas other clients may have more. There are genetic differences among individuals that cause enzymes that metabolize drugs to vary, sometimes causing drug toxicity. Some individuals may develop side effects to drugs or not respond to therapy as hoped. The future of drug therapy, related to the field of pharmacogenomics, is customized treatment that is targeted for a specific client rather than the population as a whole. When drug therapy is targeted through pharmacogenetics, it can have a significant role in identifying responders and nonresponders to medications, avoiding adverse effects, and improving drug dosing (FDA, 2023b).

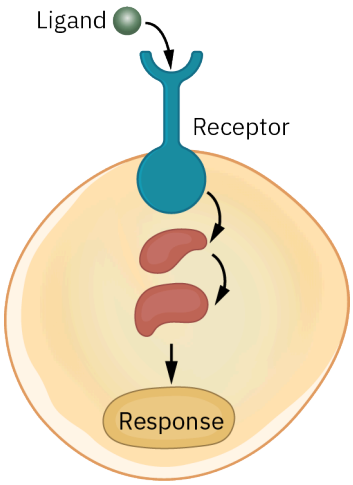


FIGURE 2.5 A cell with a receptor and ligand. Once the receptor receives the ligand, it causes a response. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Receptors are responsible for specific drug actions, affect the drug dose or concentration relationship, and mediate the actions of both agonists and antagonists. The **ligand** is a molecule that binds to a receiving protein molecule or receptor. An **agonist** is a drug that stimulates receptors to initiate a response. It mirrors the endogenous or body's internal receptor ligand to initiate the receptor to emit a biological response. An agonist has an **affinity**, or strong attraction, to a receptor and causes **intrinsic activity**, which refers to the efficacy of a drug and its ability to activate

the desired receptor. The agonist basically mimics the action of the body's physiological response. An example of this is insulin, which mimics the body's actions of endogenous insulin at receptor sites. Another example is beta-adrenergic receptors (located in the heart and kidneys), which increase heart rate, myocardial contractility, and the speed of the electrical conduction through the heart when activated by an agonist, such as the catecholamine epinephrine (adrenalin).

An **antagonist**, in contrast, binds with a receptor but does *not* activate the receptor; however, it prevents the agonist from binding to the receptor and initiating a response—in essence, it blocks or inhibits the natural or endogenous response. Antagonists may block a body's endogenous chemicals or other drugs. In contrast to the example above, beta-adrenergic blockers work by blocking endogenous catecholamines, such as the hormone epinephrine (adrenalin), thus causing the heart to beat more slowly, decreasing myocardial contractility, and decreasing the speed of conduction through the heart's electrical system. Some drugs are **partial agonists**, which have affinity and moderate intrinsic activity. A partial agonist activates a receptor but not to the extent that a full agonist does.

Mechanism of Action

The interaction between a drug and a receptor is the **mechanism of action**, or "how the drug works." This is the *way* that a drug produces its pharmacological effect. Sometimes drugs affect target cells through enzymes or by changing cell function or the cellular structure itself. Morphine, an opioid, acts directly upon mu and kappa receptors in the central nervous system and alters the perception of pain. Ibuprofen, another pain reliever, decreases pain and inflammation by inhibiting prostaglandin synthesis. Acetaminophen is thought to inhibit prostaglandin synthesis in the central nervous system, though it has no anti-inflammatory properties like ibuprofen does. (Interestingly, its exact mechanism of action is unknown.) These are three examples of pain relievers with different mechanisms of action.

Other examples of different mechanisms of action are the drugs used to treat hypertension. A thiazide diuretic reduces blood pressure by reducing circulating blood volume—to be even more specific, it increases sodium and water excretion by inhibiting the reabsorption of sodium in the distal tubule of the nephron. Compare that to the beta-adrenergic blocker metoprolol, which reduces blood pressure by blocking beta-1 adrenergic receptors at beta-adrenergic receptor sites and causes arterial vasodilation. However, it also acts to decrease blood pressure through decreased renin production. On the other hand, the angiotensin-converting enzyme blocker lisinopril reduces blood pressure through a different mechanism. It blocks the conversion of angiotensin I to the potent vasoconstrictor angiotensin II. This prevents the breaking down of bradykinin and other prostaglandins, which are vasodilatory, and decreases aldosterone production, which retains sodium and water and excretes potassium. This decrease in aldosterone production causes less sodium and water to be retained and more to be eliminated through the kidneys. This illustrates that the same effect—reduced blood pressure—can be produced by vastly different processes.

Not all drugs have a known mechanism of action. The therapeutic effect can be observed, but how the therapeutic effect occurs remains a mystery. Some examples of drugs where the exact mechanism of action is unknown include acetaminophen, cannabidiol (CBD), and the muscle relaxant cyclobenzaprine.

Side Effects, Adverse Drug Reactions, Drug Tolerance, and Drug Toxicity

Therapeutic effects are the intended, beneficial, desired effects of a drug. Sometimes a drug will have more than one therapeutic effect. Aspirin is an example of a drug with multiple therapeutic effects—it can reduce fever, pain, and inflammation. However, a drug may cause other responses that are undesirable, unintended, or secondary effects. These are known as **side effects** or **adverse drug reactions**. There are some who use these terms interchangeably, though others differentiate between the two. Side effects are secondary effects of the drug and are usually mild and predictable. Some side effects, or secondary effects, may even be desirable. Diphenhydramine is a histamine blocker. Because it has the side effect of drowsiness or sleepiness, it is sometimes used at night to occasionally aid in sleep. Adverse drug reactions may be harmful and lead to injury. These are secondary effects that are observed at therapeutic doses. Medication taken for hypertension sometimes causes hypotension, for example. Common side effects are usually mild, but some drugs have serious adverse effects that may be potentially lethal. An example of a common side effect of many drugs, including aspirin, is nausea or lack of appetite. A serious adverse drug effect of aspirin is gastrointestinal bleeding. Morphine, an opioid agonist, often has the side effect of constipation. However, respiratory depression is an adverse drug reaction sometimes seen with

the administration of morphine and can lead to harm to client.

Drug **tolerance** occurs when a client requires more drug (or higher concentrations) in order to achieve the desired effect. Nitrates for chest pain sometimes cause tolerance. Essentially, the body becomes used to the medication, and more drug may be needed to get the desired effect, or a different drug has to be used. For nitrates, the client needs to have a period of time without the drug, so providers may order the drug for daytime use but withhold the drug during the night. Another common example is the use of opioids. At high doses, this class of medications causes euphoria and pleasure, but over time if the individual continues to take the drug, the euphoria and pleasure produced by the drug decrease. Initially, the client might find pain relief when taking only 5 mg of oxycodone; however, with continued use over time, higher and higher doses are required in order to achieve the same effects. Drug **dependence** occurs when the body develops a physiological or psychological need for a drug. The physiological need means that the drug's absence may cause physical withdrawal symptoms if the drug is not taken. Psychological dependence is observed by an intense urge to have the drug despite the adverse consequences of taking the drug.

Drug toxicity can occur when there is an excess accumulation of a drug in the system. The ingestion of an excessive amount of a drug might cause toxicity; however, even therapeutic doses of some drugs may cause toxicity in some clients. Drug concentrations can also accumulate if drug-metabolizing organs are not functioning properly and the dose is not adjusted accordingly. A client who has liver or kidney dysfunction may be at risk for drug toxicity. When a client with liver dysfunction is given a drug that is metabolized in the liver, the dosage may need to be decreased to prevent the accumulation of the drug in the body. The same is true for a client with kidney dysfunction. If the drug is excreted through the kidneys, then the dosage and frequency of the drug will need to be modified. A drug excreted by the kidneys will usually be safe for the client with liver dysfunction, and vice versa.

2.3 Drug Administration Routes, Preparation, and Administration

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 2.3.1 Identify the different routes of drug administration.
- 2.3.2 Discuss sites for parenteral therapy.
- 2.3.3 Analyze nursing interventions related to drug administration.
- 2.3.4 Explain equipment and techniques for drug administration.

This section will discuss the different routes for medication administration, how to prepare for administration, and the various methods for administering drugs to the client. Both **enteral** and **parenteral** sites will be reviewed, along with the equipment needed for each type of drug administration. Techniques for drug administration will be described.

Forms and Routes of Drug Administration

There are many different forms of medication: liquid, suspensions, tablets, capsules, lotions, and ointment, to name a few. There are also many routes through which medications can be given and absorbed into the body. The routes of medication administration are broadly categorized as follows:

- *Enteral administration:* "Enteral" means "pertaining to the intestines." Most enteral medications are absorbed in the intestines. The primary routes for enteral administration are oral and, to a lesser extent, rectal. Some clients have tubes placed directly into the gastrointestinal tract (e.g., nasogastric tubes or percutaneous endoscopic gastrostomy [PEG] tubes). Absorption will vary, but all will be affected by the first-pass effect.
- *Parenteral administration:* "Parenteral" refers to any drug that is administered outside of the GI tract; however, it most commonly refers to injectable drugs administered via the subcutaneous, intramuscular, or intravenous routes. Drugs administered via these routes have improved bioavailability because they bypass the first-pass effect, making absorption and onset of action more rapid.
    - *Percutaneous administration:* Some sources will define percutaneous administration as a separate category or a subcategory of parenteral routes. The percutaneous route refers to topical drugs absorbed through the skin—lotions, ointments, creams, or patches.

The following sections describe the equipment needed for the administration of medications. The various techniques of each route are detailed, along with their pertinent advantages and disadvantages. Nursing

implications are also covered in relation to each route of administration.

SAFETY ALERT

Medication Safety

The following are some tips for medication safety:

- It is best practice to prepare medications for only one client at a time. This safety practice reduces the risk of inadvertently administering medications to the incorrect client.
- Medications that require a focused assessment or monitoring should be kept separate from other medications. For example, if administering a medication that lowers blood pressure and heart rate, vital signs should be assessed before giving the drug. Because opioids may cause respiratory depression, respiratory rate and oxygen saturation should be assessed before and after administration of the drug.
- All unit-dose medications should be opened at the bedside rather than in the medication room.
- Never leave medications unattended at the bedside unless specifically ordered. Remain with the client until all medications have been administered.

Product (Drug) Labeling

Each prescription drug includes a package insert that provides clients with information about the drug. Many package inserts are developed by the manufacturer and approved by the FDA for use by clients and caregivers (FDA, 2023a). Some of the information contained in the inserts includes generic and trade names, routes, instructions for taking the drug, and how to store and dispose of the drug. Any side effects, especially if the drug has serious side effects, are listed, as are directions about what to do if adverse effects occur. General information about the safe use of the drug, how to report side effects, and ingredients are also listed. These package inserts are often one of the best resources for free information for the client.

Oral Medications

Oral administration encompasses several different drug forms. Liquids, elixirs, suspensions, tablets, capsules, and caplets may all be given orally. Oral administration is usually quick, easy, and convenient, but the onset of action is longer and unpredictable due to the first-pass effect, and not all drugs can be administered this way. Table 2.1 lists the advantages and disadvantages of oral administration.

Advantages	Disadvantages
• More convenient for the client (it can be done at home) • Usually less expensive compared to parenteral forms • Usually safe for most clients	• Variable absorption, with some oral drugs having poor absorption • Undergoes first-pass effect • Some drugs are destroyed in the acidic environment of the stomach; the absorption of some drugs may vary significantly in the presence or absence of food • Cannot be given if the client is nauseated or vomiting or has decreased GI motility • May be aspirated • Cannot be given to clients who have difficulty swallowing (stroke) or are unconscious • Clients must be cooperative

TABLE 2.1 **Advantages and Disadvantages of Oral Administration**

Steps to administering an oral medication:

1. Assemble the appropriate equipment:
    - Drinking cup
    - Straw
    - Disposable medication cup (souffle cup or calibrated plastic medication cup for liquids)

2. Assess the client to determine if the drug is safe and appropriate to give.
3. Check the medication, dose, and expiration date.
4. Check NPO status and ensure the client does not have nausea or vomiting. (NPO is a Latin term meaning *nil per os*, or nothing by mouth. Sometimes this will include medications.)
5. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
    - During verification of the contents of the medication administration record and the orders
    - When preparing the medication
    - At the bedside
6. Wait to open blister packs or oral unit doses until at the client's bedside.
7. Perform hand hygiene.
8. Don gloves if you anticipate touching the pill or the client's mouth during administration.
9. Identify the client, and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the blister pack using the protocol recommended by the institution.)
    - Perform the third medication check at the bedside. This check is completed by verifying that the medication name, dosage, route, and time match the medication administration record (this is the last opportunity to prevent an error from occurring). Most institutions now have barcode scanning at the bedside as an additional layer of security.
10. Explain the medication to the client:
    - Name (brand and generic)
    - Dosage
    - Indication, rationale, or reason for the drug to be given
    - Frequency
    - Route
    - Adverse effects
11. Position the client in an upright position or on side as condition allows.
12. Assess the client's ability to swallow and the gag reflex by offering a sip of water.
13. Ask the client if they prefer all medications at once or one or two at a time.
14. Give the client the medication with a cup of water (approximately 8 ounces unless the client is on a fluid restriction).
15. Document administration within the medication administration record (MAR).
16. Perform hand hygiene.
17. Evaluate the client's response to the drug(s) within the appropriate time frame.

Nursing Implications for Oral Medications

The nurse should do the following for clients who are taking oral medications:

- If a tablet needs to be split, split only tablets that are scored. If a client has difficulty swallowing a tablet or capsule, consult a pharmacist for advice about the technique of administration because some capsules may be opened and emptied into a food or liquid. Timed-release capsules or tablets should *not* be crushed or chewed because this may affect the rate of absorption and toxicity may occur. For this reason, timed-release capsules should *not* be opened and emptied into food for ease of swallowing.
- Use a hospital-approved device to split the tablet. (Some health systems split the tablets in the pharmacy and send them to the unit in unit-dosed packaging for safety purposes.)
- Discard any unused portion according to institutional policy.
    - If the drug is a controlled substance, document the waste with another nurse in the medication room.
- If a tablet needs to be crushed:
    - Ensure that it can be crushed.
    - *Never* crush sustained-release, extended-release, or enteric-coated tablets.
    - If crushing more than one tablet, keep them separate; do not combine them.
- When filling a calibrated plastic cup with liquids, fill at eye level.
- Always remain with the client until all medications are taken; do not leave drugs at the bedside unattended.

Sublingual and Buccal Administration

Absorption of sublingual medications occurs in the area under the tongue, whereas buccal medications are absorbed in the oral mucosa, generally between the cheek and gums. These are vascular areas, and medications administered here are absorbed rapidly because they do not undergo the first-pass effect. Table 2.2 lists the advantages and disadvantages of sublingual and buccal administration.

Advantages	Disadvantages
• Convenient • Rapidly absorbed • Very rapid onset of action • Avoids first-pass effect • Advantageous for clients who cannot swallow tablets	• May interfere with drinking, talking, or eating • May be unpalatable • Few drugs available in this form • May be irritating to the oral mucosa

TABLE 2.2 **Advantages and Disadvantages of Sublingual/Buccal Administration**

Steps to administering a sublingual or buccal medication:

1. Assemble the appropriate equipment:
    - Disposable medication cup (souffle cup)
    - Drinking cup
    - Straw
2. Assess the client to determine if the drug is safe and appropriate to give.
3. Check the medication, dose, and expiration date.
4. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
    - During medication reconciliation
    - When preparing the medication
    - At the bedside
5. Perform hand hygiene.
6. Don gloves if you anticipate touching the pill or the client's mouth during administration.
7. Identify the client, and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the blister pack, using the protocol recommended by the institution.)
8. Perform the third medication check at the bedside.
9. Explain the medication to the client:
    - Name (brand and generic)
    - Dosage
    - Indication, rationale, or reason for the drug to be given
    - Frequency
    - Route
    - Adverse effects
10. Offer sips of water to moisten the oral cavity.
11. Assist the client in placing the medication sublingually (or between the cheek and gum for buccal drugs).
12. Instruct the client to allow the medication to dissolve completely. Discuss the importance of not swallowing or chewing the pill.
13. Educate the client about the importance of abstaining from food, drinking, or smoking until after the medication has dissolved.
14. Document administration within the MAR.
15. Perform hand hygiene.
16. Evaluate the client's response to the drug(s) within the appropriate time frame.

Nursing Implications for Sublingual or Buccal Medications

The nurse should do the following for clients who are taking sublingual or buccal medications:

- Always remain with the client until all medications are taken; do not leave drugs at the bedside unattended unless the provider has ordered the medication to be left at the bedside.

- Exception: Sublingual nitroglycerin tablets or sprays are often ordered to be left at the bedside so that a client may take them as needed in the event of chest pain.

Nasal Spray Administration

Nasal sprays can be rapidly absorbed into the mucous membranes of the nasal cavity. Table 2.3 lists the advantages and disadvantages of nasal sprays.

Advantages	Disadvantages
• Convenient • Rapidly absorbed • Very rapid onset of action • Avoids first-pass effect • May affect taste	• Few drugs are available in this form • May be irritating to the nasal mucosa • Aseptic technique should be used due to the connection between the nasal cavity and sinuses • Some nasal sprays, such as oxymetazoline for congestion, should be used for only 3–5 days; rebound congestion may occur if used beyond that time

TABLE 2.3 **Advantages and Disadvantages of Nasal Sprays**

Steps to administering a nasal spray:

1. Assemble the appropriate equipment:
   - Clean gloves
   - Tissue
   - Medication
2. Assess the client to determine if the drug is safe and appropriate to give.
3. Check medication, dose, and expiration date.
4. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
   - During medication reconciliation
   - When preparing the medication
   - At the bedside
5. Educate the client.
   - Explain the method for administering the medication. (This route may be self-administered in the future; however, the nurse should observe this in order to provide appropriate documentation in the MAR.)
   - Inform the client that they may experience a burning or stinging sensation with administration.
6. Instruct the client to gently blow their nose (unless it is contraindicated for the client).
7. Assess the nostrils for erythema, edema, drainage, or tenderness.
8. Client should be upright in a sitting position with their head tilted back.
9. Block one nostril.
10. Hold the medication bottle upright and shake.
11. Immediately insert the tip of the applicator into the nostril.
12. Ask the client to inhale while simultaneously squeezing a spray into the nostril.
13. Once the bottle has been squeezed to deliver the medication, do not release the squeeze until the spray bottle has been removed from the nares. Ensure that the nozzle of the nasal spray does not touch the nasal turbinates or septum because pain or injury could occur.
14. Repeat the process in the other nostril if indicated.
15. Have tissue available if needed to blot the nostril. The client should avoid blowing their nose immediately.
16. Wipe the spray applicator with a clean, dry cloth or tissue.
17. Remove gloves and perform hand hygiene.
18. Document administration within the MAR.
19. Evaluate the client's response to the drug(s) within the appropriate time frame.

Be aware that some nasal medications may vary from this procedure; it is important to consult the product labeling to confirm the appropriate administration technique.

Nursing Implications for Nasal Sprays

The nurse should do the following for clients who are taking nasal sprays:

- Do not readminister the drug if the client sneezes following the administration of the nasal spray because there is no way to assess how much of the drug has been absorbed.

Removing Parenteral Medication from a Vial

When administering a parenteral medication, such as a subcutaneous or intramuscular injection, it is important to remember that this is an invasive procedure (a needle is inserted into the client). The medication may come in a prefilled syringe; however, it is usually drawn up by the nurse from a vial of medication. The nurse should be very alert during the process of drawing up and administering the medication to keep the needle and contents sterile.

Steps to withdrawing medication from a vial:

1. Perform hand hygiene and don clean gloves (not sterile).
2. Inspect and verify the medication, dose, volume, and expiration date.
3. Verify the dosage calculation.
4. Remove the plastic cap from the top of the unused vial with a flick of the thumb.
5. Wipe the rubber stopper or port with an alcohol swab and allow it to air dry for approximately 10 seconds.
    - The cap does not keep the top of the port sterile. Dust and microbial contaminants can collect under the cap, so it is important to cleanse with alcohol.
6. Insulin and tuberculin syringes have preattached needles. If drawing up insulin, insulin syringes have preattached needles with orange caps (see Figure 2.6). Insulin syringes are marked in unit measures rather than in milliliters (mL). The needles on these syringes are fragile and bend very easily, so it is important to be careful when inserting and withdrawing the needles from the vial.
7. When drawing up medications into syringes that are not insulin or tuberculin syringes:
    a. Attach a blunt-tipped needle to the syringe of choice. The syringe choice should be large enough to hold the dose of medication, but the smallest syringe closest to that measurement (i.e., if administering 4 mL, draw it up in a 5 mL syringe rather than a 10 mL, 20 mL, etc.).
    b. Remove the needle cap and draw air into the empty syringe to the volume of medication to be given (e.g., if giving 2 mL of medication, then draw up 2 mL of air).
    c. Insert the air into the vial of medication through the center of the rubber port at the top of the vial.
        - Ensuring that the tip of the needle is above the fluid level of the vial will help avoid the presence of bubbles. (It prevents agitation of the drug.)
        - Be sure to maintain the sterility of the needle.
        - Do not touch the needle.
        - Be careful not to bend the needle.
    d. Inject the air into the vial.
    e. Invert the vial and hold it at eye level to slowly withdraw the desired volume of medication.
        - If the medication is withdrawn too quickly, air bubbles may enter the syringe.
        - *Important tip:* Ensure that the tip of the needle is below the fluid level in the vial so that no air is drawn into the syringe.
        - Withdraw slightly more of the medication than needed.
        - Express any air bubbles and the excess medication back into the vial until the desired amount of medication is in the syringe.
        - Withdraw the needle from the vial, being careful not to bend the needle.
        - Exchange the blunt needle for a regular needle prior to administration.

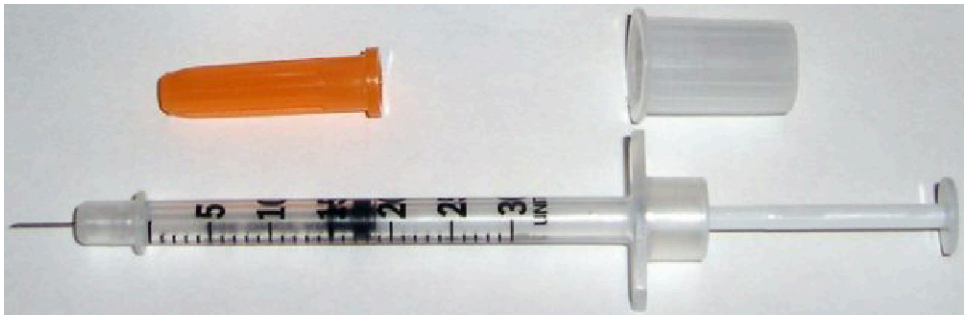


FIGURE 2.6 An insulin syringe has a pre-attached needle and an orange cap. (credit: modification of work "Standard insulin syringe" by Matanya/Wikimedia Commons, Public Domain)

Removing Medication from Ampules

Steps to withdrawing medication from an ampule:

1. Wash hands and don clean gloves.
2. Medication may be seen in both the bottom and top portion of the ampule (see Figure 2.7). Thump or flick the top of the ampule to bring the medication to the bottom portion of the ampule.

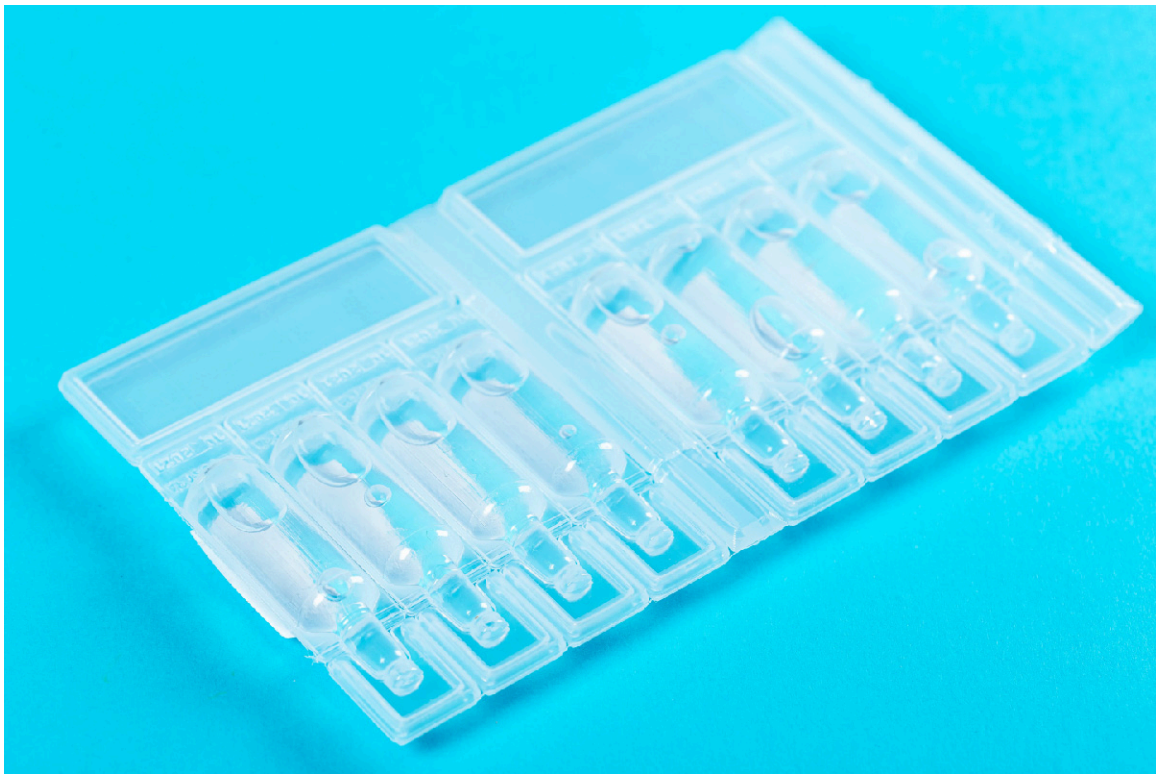


FIGURE 2.7 An example of what an ampule looks like; note the top and bottom portion. (credit: "Group of modern plastic ampules on blue background (https://openstax.org/r/ampules)" by Marco Verch/Flickr, CC BY 2.0)

3. Place an unopened alcohol swab packet or gauze pad between the thumb and fingers and wrap around the neck of the glass ampule. Snap the neck quickly and firmly *away* from you (and anyone around you).
4. Dispose of the top of the ampule in a sharps container.
5. Attach a blunt filter needle to the appropriate syringe.
6. Remove the cap of the filter needle and insert the needle into the center of the opened ampule, being careful to avoid touching the rim of the ampule with the needle.
7. *Do not* inject air into the ampule.
8. Gently pull back on the plunger to draw the medication into the syringe, keeping the needle tip in the fluid. The ampule can be tipped to the side to aid in the process of drawing the medication into the syringe.
9. If bubbles are aspirated into the syringe, do not expel the bubbles back into the ampule. Simply remove all of the fluid, withdraw the needle, and hold the syringe in a vertical position (at a 90-degree angle). Tap the side

of the syringe to move the air bubbles to the top of the syringe and expel the excess air without wasting the medication.

10. Scoop the needle cap onto the needle, twist and remove the filter needle from the syringe, and dispose of the filter needle in a sharps container.
11. If the volume in the syringe is greater than needed, discard according to institutional policy.
12. Place a sterile tip or the appropriate needle for parenteral administration onto the syringe.
13. *Do not* administer the medication using the filter needle used to draw up the medication.
14. Proceed with labeling and administering the medication according to the administration technique needed.

SAFETY ALERT

Filter Needles

Never inject a medication into a client using a filter needle. A filter needle is used to remove any microscopic glass particles that might occur as a result of ampule breakage. This has the potential of administering these glass fragments into the client.

Subcutaneous Administration

Subcutaneous injections are administered "under the skin" into the adipose tissue between the dermis and muscular layer (see Figure 2.8). Clients can be instructed to self-administer injections subcutaneously. Common medications administered within this layer are enoxaparin, heparin, and insulin. Medication administered here is often absorbed slowly due to the reduced number of blood vessels in this area. There are many potential sites for subcutaneous injections: upper arms, thighs, abdomen, back, and buttocks. The specific sites for each drug are usually detailed in the drug's package insert or labeling. Routine injections should be rotated regularly among the different sites. Do not inject into sites that are hard when palpated. Do not rub the injection site, though gentle pressure may be applied to the area after the drug has been administered.

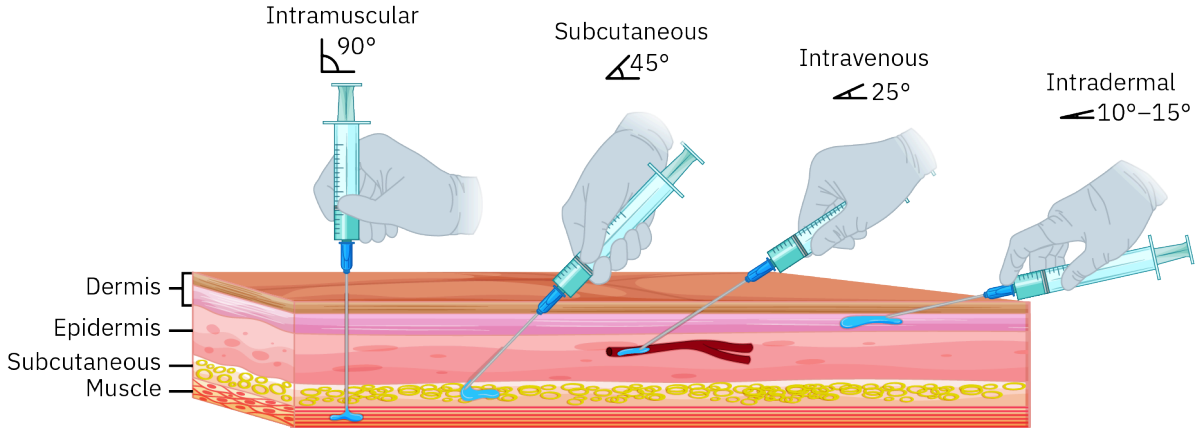


FIGURE 2.8 Different types of injections require different angles of injection. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Table 2.4 lists the advantages and disadvantages of subcutaneous administration.

Advantages	Disadvantages
• Absorption is slower than with IM injections, but the duration of action is longer • Can be self-administered by the client • Low risk of infection	• Maximum volume of medication via this route is 1.5 mL • Absorption varies from site to site

TABLE 2.4 Advantages and Disadvantages of Subcutaneous Administration

Steps to administering a subcutaneous medication:

1. Assemble the appropriate equipment:
    - Medication

- Sterile syringe (1–3 mL)
- Small-gauge needles (3/8–5/8 inch) (tuberculin and insulin syringes have preattached needles)
- Alcohol swabs
- Gloves (clean gloves, not sterile)

2. Assess the client to determine if the drug is safe and appropriate to give.
3. Check the medication, dose, volume, and expiration date.
4. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
   - During medication reconciliation
   - When drawing up the medication
   - At the bedside
5. Perform hand hygiene.
6. Don gloves.
7. Identify the client, and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the vial or unit dose, using the protocol recommended by the institution.)
8. Perform the third medication check at the bedside.
9. Explain the medication to the client:
   - Name (brand and generic)
   - Dosage
   - Indication, rationale, or reason for the drug to be given
   - Frequency
   - Route
   - Adverse effects
10. Prepare medication using the correct needle length (3/8–5/8 inches), gauge (25–29 gauge), and syringe (usually no more than 1.5 mL can be given via this route). For clients with little adipose tissue, use the smaller needle.
11. Select an injection site with an adequate fat pad.
    - Avoid bruises, rashes, inflammation, or areas of injury.
    - Ensure that the injection site is a *minimum* of 2 inches away from the umbilicus, a stoma, or an incision.
    - Preferred sites include the abdomen, upper arms, and anterior thighs.
12. Assist the client into a position in which the site or extremity can be relaxed.
13. Cleanse the area with an alcohol swab using a circular motion by starting at the center and working outward in a widening circle to about 2–3 inches. Allow to air dry.
14. Grasp the skinfold between your thumb and index or third finger of the nondominant hand. (A new alcohol swab or gauze can be placed between the fourth and fifth fingers of this hand to use after injection.)
15. Remove the needle cap carefully and dispose.
16. Instruct the client that they will feel a "pinch."
17. Quickly and smoothly insert the needle into the skin and adipose tissue at a 45- to 90-degree angle. The anticoagulant enoxaparin is a subcutaneous injection that should be given at a 90-degree angle.
18. Inject the medication with the dominant hand depressing the plunger with slow and even pressure, while holding the barrel of the syringe steady with the nondominant hand.
19. Do *not* aspirate for subcutaneous injections.
20. Withdraw the needle smoothly *at the same angle* that it was inserted to prevent trauma at the injection site.
21. Apply gentle pressure with the alcohol swab, but do not massage the site, especially if the medication given was an anticoagulant such as heparin or enoxaparin, because this may cause extensive bruising.
22. Activate the safety device on the syringe and dispose of the syringe in the sharps container or a puncture-resistant needle disposal container according to institutional policy. Never throw it into the trash.
23. *Do not recap the needle!* This is a safety hazard for the nurse. Recapping needles may lead to needle sticks and exposure to pathogens.
24. Remove gloves and perform hand hygiene.
25. Document in the MAR. When documenting a subcutaneous injection, be sure to document the site the

medication was administered to allow for the rotation of sites.
26. Evaluate the client's response to the drug(s) within the appropriate time frame.

Nursing Implications for Subcutaneous Administration

The nurse should do the following for clients receiving a subcutaneous injection:

- For heparins and insulins: Both are high-alert medications. A second nurse will need to verify the dose. Do not draw up the dose until a witness is available to verify.
- Never draw heparin up into an insulin syringe. (Fortunately, many heparins come in prefilled syringes for safety reasons.)
  - Insulin, and only insulin, should be drawn up into an insulin syringe. *Never* draw up insulin into a regular syringe with milliliter (mL) markings because this will cause an overdose of insulin.
- Administer subcutaneous injections at a 45- to 90-degree angle depending upon the body habitus of the individual. For extremely thin individuals and children, ensure that the angle is shallow enough that the medication is not given intramuscularly

LINK TO LEARNING

ISMP Guidelines for Safe Subcutaneous Insulin Use

Review the ISMP Guidelines for Optimizing Safe Subcutaneous Insulin Use in Adults (https://openstax.org/r/ismpsites). According to the Institute for Safe Medication Practices (ISMP), insulin is associated with more medication errors than any other type or class of drugs.

Intramuscular Injections

Intramuscular injections (IM) are administered deep into the muscular tissue beneath the dermis and subcutaneous layers (see Figure 2.9). The most common sites for IM injections are the ventrogluteal and deltoid areas. Vastus lateralis landmarks are preferred for infants and children under age 2. Table 2.5 lists the advantages and disadvantages of intramuscular administration.

Advantages	Disadvantages
• Absorption is more rapid than with subcutaneous injections. • Rapid onset of action • Avoids first-pass effect	• Maximum volume of medication via ventrogluteal route is 3 mL (If more than 3 mL is required, separate into two injections.) • Incorrect placement of the needle may cause harm to the client (nerve or blood vessel injury) • Some drugs are very irritating to the tissues, which causes pain • Drug absorption is variable (depends on the muscle group) • Painful

TABLE 2.5 **Advantages and Disadvantages of Intramuscular Administration**

Steps to administering an intramuscular medication:

1. Assemble the appropriate equipment:
   - Medication
   - Syringe (3 mL)
   - Needles (unless preattached)
   - Alcohol swabs
   - Gloves (clean gloves, not sterile)
2. Assess the client to determine if the drug is safe and appropriate to give.
3. Check the medication, dose, volume, and expiration date.
4. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).

- During medication reconciliation
- When drawing up the medication
- At the bedside

5. Perform hand hygiene.
6. Don gloves.
7. Identify the client, and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the vial or package, using the protocol recommended by the institution.)
8. Perform the third medication check at the bedside.
9. Explain the medication to the client.
   - Name (brand and generic)
   - Dosage
   - Indication, rationale, or reason for the drug to be given
   - Frequency
   - Route
   - Adverse effects
10. Prepare medication using the correct needle length (1–1.5 inches), gauge (18–27 gauge), and syringe (no more than 3 mL can be given via the ventrogluteal route, and no more than 1 mL can be given in the deltoid). (See Figure 2.9.)
11. Select an injection site.
    - Avoid areas of hardness, bruising, rashes, inflammation, injury, or infection.
    - Assess muscle size and integrity.
12. Assist the client into a position in which the site or extremity can be relaxed.
13. Cleanse the area with an alcohol swab using a circular motion by starting at the center and working outward in a widening circle to about 2 inches. Allow to air dry for 10 seconds.
14. Remove the needle cap carefully.
15. Instruct the client that they will feel a "stick."
16. Grasp the syringe like a dart with the dominant hand.
17. Quickly and smoothly insert the needle through the skin and adipose tissue to the muscular layer at a 90-degree angle.
18. Inject the medication with the dominant hand depressing the plunger with slow and even pressure, while holding the barrel of the syringe near the hub steady with the nondominant hand.
19. Withdraw the needle smoothly at the same angle that it was inserted.
20. Apply gentle pressure with the alcohol swab, but do not massage the site.
21. Activate the safety device on the syringe and dispose of the syringe in the sharps container or in a puncture-resistant needle disposal container according to institutional policy. Never throw it into the trash.
22. *Do not recap the needle!* This is a safety hazard for the nurse. Recapping needles may lead to needle sticks and exposure to pathogens.
23. Remove gloves and perform hand hygiene.
24. Document in the MAR. When documenting an IM injection, be sure to document the site the medication was administered to allow for the rotation of sites if other doses are necessary.
25. Evaluate the client's response to the drug(s) within the appropriate time frame.

FIGURE 2.9 Needles come in a variety of gauges and lengths. The larger the number of the gauge, the smaller the needle. The number designating the length of the needle will be the actual length of the needle in inches. (credit: "Needles of various gauge and length" by Sean/Rx-wiki, CC BY 3.0)

Follow institutional policy about aspiration with IM injections. The Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) no longer recommend the practice of aspiration for vaccinations because no large blood vessels lie close to the area of injection (CDC, 2023). It is thought that it may cause pain at the site if the syringe is not stable and may actually cause damage to the tissue. At this point in time, there is not enough evidence-based information to support or abort the process of aspiration. Most studies look at the potential discomfort felt with aspiration rather than the safety of intramuscular administration. If the institution recommends aspiration, follow these steps:

1. Quickly and smoothly insert the needle through the skin and adipose tissue into the muscular layer at a 90-degree angle.
2. With the dominant hand, pull back on the plunger to aspirate for blood return for 5 seconds. If blood enters the hub of the needle/syringe, stop. Pull the needle out and begin again using a new needle and a different site.
3. If no blood return is seen with aspiration, inject the medication with the dominant hand depressing the plunger with slow and even pressure, while holding the barrel of the syringe near the hub steady with the nondominant hand.
4. Continue, using the instructions above.

Z-Track Method

Some institutions require all IM injections to be given with the Z-track method. It is particularly helpful with medications that stain the skin or are irritating, such as iron preparations. The Z-track method is never wrong, but it isn't always necessary. For this reason, know the institutional policy and proceed accordingly.

1. Use the nondominant hand to displace the skin tissue laterally approximately 1 inch.
2. Hold the tissue laterally and insert the needle.
3. Gently inject the medication into the muscle and wait 10 seconds.
4. Remove the needle and then release the skin and allow it to return to its normal position after withdrawing the needle.

Deltoid Injections

To give a **deltoid** injection, remove clothing to expose the upper arm and shoulder area. Discuss the preferred arm with the client. They may prefer the nondominant arm to be used due to potential soreness; however, many individuals prefer the dominant arm because the increased movement with that arm may work the soreness out earlier. The client may bend the elbow to assist with relaxation of the muscle. To determine landmarks, find the acromion process, which will be the base of an upside-down triangle. Locate the lateral midpoint on the arm in line

with the axilla. The injection site will be located in the center of the triangle, approximately 1.5 inches below the acromion process. (See Figure 2.10.)

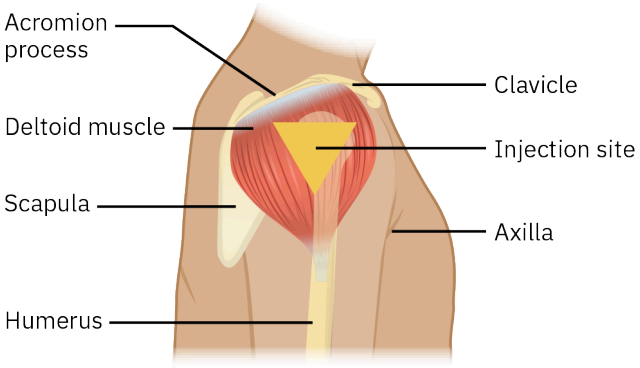


FIGURE 2.10 The deltoid injection site is located within the triangle shown here. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

LINK TO LEARNING

Deltoid Injections

Access multimedia content (https://openstax.org/books/pharmacology/pages/2-3-drug-administration-routes-preparation-and-administration)
Watch this video to see a nurse demonstrate the technique for administering an IM injection in the deltoid muscle using the Z-track technique.

SAFETY ALERT

Needle Disposal

Never dispose of needles in trash cans. Needles should be disposed of in a sharps disposal container. These containers are made from rigid, puncture-resistant plastic or metal and have a tight-fitting lid that allows disposal of the sharp without allowing the hand or fingers to enter. These containers limit the potential of exposure to blood-borne pathogens from used needles. Once full, the containers should be entrusted into the care of a hazardous waste management company to ensure proper disposal.

Ventrogluteal Injections

To give an injection at the **ventrogluteal** site, position the client on their side with the knees bent (upper leg slightly ahead of the lower leg). Use the left hand to find landmarks when injecting into the right ventrogluteal site, and use the right hand to find landmarks when injecting into the left ventrogluteal site. Locate the greater trochanter at the head of the femur and place the palm of the hand over the greater trochanter and the index finger on the anterosuperior iliac spine. Aim the middle finger and ring finger toward the iliac crest. Point the thumb toward the client's groin with the fingers toward the client's head. Spread the middle finger along the iliac crest toward the buttocks. The injection site is in the center of the triangle formed by the middle and index fingers. (See Figure 2.11.)

LINK TO LEARNING

Ventrogluteal Injections

Access multimedia content (https://openstax.org/books/pharmacology/pages/2-3-drug-administration-routes-preparation-and-administration)
Watch this video to see a nurse demonstrate how to use body landmarks to identify the location for a ventrogluteal injection, and then the correct technique for administering an IM medication at this site.

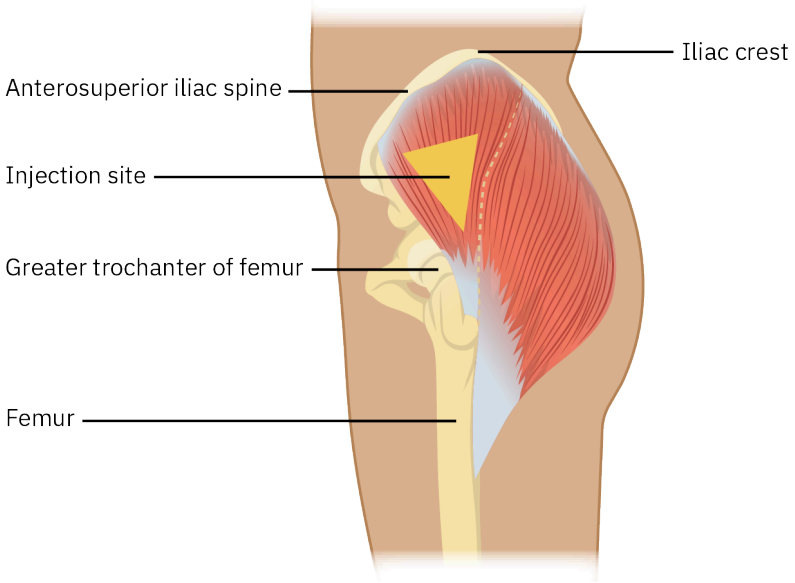


FIGURE 2.11 The proper placement for determining the injection site for a ventrogluteal IM injection. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Intravenous Push (IVP) Administration via Saline Lock

Intravenous medications are introduced directly into the vein and, thus, into the circulation during administration. This route is the fastest because no absorption is necessary, and drugs are 100% bioavailable because they bypass the first-pass effects of the liver. Table 2.6 lists the advantages and disadvantages of IVP administration.

Advantages	Disadvantages
• Very fast absorption and onset of action • Useful in emergencies • Medications are delivered systemically • Drugs may be delivered both intermittently and continuously • Once the IV has been established, it is usually more comfortable for the client • Predictable drug levels	• Often more expensive • Clients may be less mobile • Risk for infection (more invasive) • When adverse effects occur, they may be more severe • Risk of phlebitis (inflammation of the vein due to mechanical or chemical irritation) • Risk of infiltration/extravasation (The IV catheter is no longer in the vein; the medication infuses into the tissue instead. Extravasation is related to medication that is harmful to the tissue—in fact, it may cause tissue death.)

TABLE 2.6 Advantages and Disadvantages of IVP Administration

Steps to administering an IVP medication:

1. Assemble the appropriate equipment:
    - Medication
    - Syringe with a needleless device
    - Needles
    - Normal saline flushes
    - Diluent, if needed
    - Alcohol swabs
    - Gloves
2. Assess the client to determine if the drug is safe and appropriate to give.
3. Check the medication, dose, volume, and expiration date.
4. Check the compatibility of the medication with the IV fluids that are hanging.
5. Double-check dosage calculations.

6. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
    - During medication reconciliation
    - When drawing up the medication
    - At the bedside
7. Perform hand hygiene.
8. Don gloves.
9. In the medication room (or possibly the client's room in some institutions), use aseptic technique to draw the medication into the syringe as described in the previous section.
    a. Use a syringe size closest to the amount of the drug needed (e.g., a 3 mL syringe to draw up 1–3 mL or a 5 mL syringe to draw up 4–5 mL).
    b. Double-check the rate of administration.
    c. Label the medication syringe with the client's name, date of birth, medication name, dosage *and* volume, time, and initials. (This may vary slightly between institutions.)
10. Once in the client's room, identify the client, and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the vial or package, using the protocol recommended by the institution.)
11. Perform the third medication check at the bedside.
12. Explain the medication to the client:
    - Name (brand and generic)
    - Dosage
    - Indication, rationale, or reason for the drug to be given
    - Frequency
    - Route
    - Adverse effects
13. Assess the IV site. Check for redness, swelling, or tenderness. Assess local skin temperature for warmth.
14. Unclamp the saline lock and expel air bubbles from a saline flush. Then remove the disinfecting cap from the port.
15. Scrub the hub of the port and the threads with an alcohol swab or the institution's preferred cleanser for 15 seconds.
16. Remove the tip from the flush (see Figure 2.12) and insert the saline flush by twisting and pushing to the right. Once the flush is engaged with the saline lock, gently aspirate for blood return to assess for patency of IV.

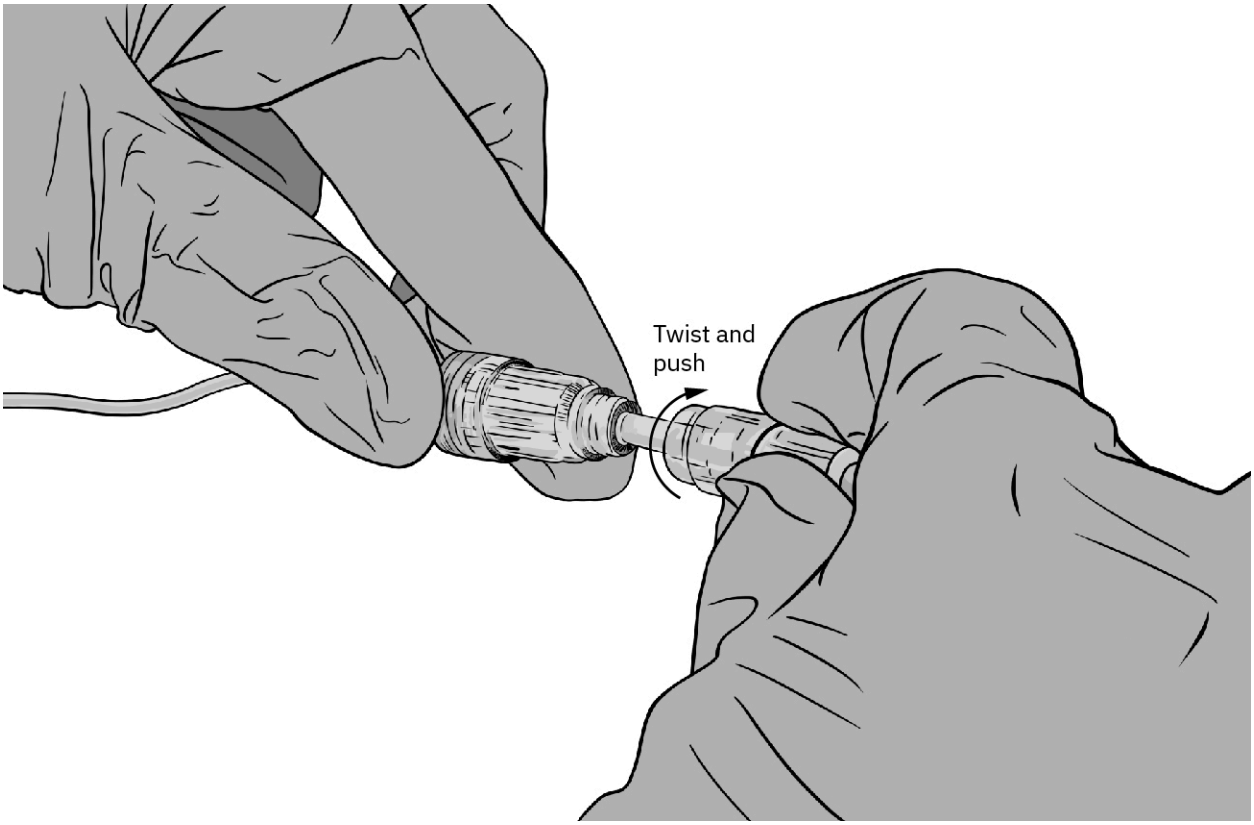


FIGURE 2.12 A syringe is attached to a saline lock by twisting and pushing to the right. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

17. Using gentle force, attempt to flush the IV with 2–3 mL of saline to assess for IV patency. If resistance is felt, *do not force*! Stop flushing immediately because the catheter may be occluded. The saline lock may need to be restarted.
18. If the catheter flushes easily, disconnect the flush from the saline lock, keeping the hub of the saline lock sterile. Keep the tip of the used saline flush sterile while attaching the syringe of medication to the saline lock. If the hub is dropped and no longer sterile, wipe the hub thoroughly for 15 seconds before attaching the syringe with the drug in it.
19. Administer the medication in a smooth, continuous manner through the saline lock at the recommended rate of administration for that particular drug until the appropriate dose is given.
20. Remember that IV medications have 100% bioavailability and an immediate onset of action. It is important to assess for adverse reactions during and after administration.
21. Disconnect the syringe and reconnect the saline flush. (Ensure that the tip is still uncontaminated.) Infuse 2–3 mL of saline through the saline lock at the same rate of infusion that the drug was given (medication is still in the saline lock) to clear the remainder of the drug from the line.
22. Place a new disinfecting cap on the port per institutional policy.
23. Remove gloves and perform hand hygiene.
24. Document in the medication administration record.
25. Evaluate the client's response to the drug(s) within the appropriate time frame.

SAFETY ALERT

IV Administration

If white, cloudy particles appear in the saline lock during administration, immediately stop administering the IV drug. This is a precipitate usually caused by incompatibility between the drug being administered and the solution in the IV line or saline lock. Some drugs may harm the client when used together. Often this is due to a chemical alteration that occurs when used concurrently. Some incompatibilities cause a precipitate or crystals to

form; others cause an inactivation of the drug; yet others may cause a toxic solution to form. Immediately clamp the IV or saline lock. Change the administration tubing and restart the infusion. Double-check for Y-site compatibility (when a drug is administered into a Y-site connection with another solution) between the solution and the medication.

Transdermal Patch (or Disk) Application

Transdermal patches are applied to the skin. Patches usually allow for a slow, very controlled release of medication into the skin over a period of hours to days. Common medications that are delivered via this route are nitroglycerin (for angina), fentanyl (for pain), and clonidine (for hypertension). Each drug delivery system is unique, so it is important to read about the individual drug to know the onset and duration of action for the medication delivered by a patch. Table 2.7 lists the advantages and disadvantages of transdermal administration.

Advantages	Disadvantages
• Medications are delivered systemically • A constant amount of medication is delivered for a specific time frame (e.g., fentanyl patches may deliver 25 mcg per hour for 72 hours) • Therapeutic effects last longer	• Patches are expensive • The rate of absorption may be affected by excessive perspiration and body temperature • If adverse effects occur, the drug continues to be absorbed even when removed from the body

TABLE 2.7 **Advantages and Disadvantages of Transdermal Administration**

Steps to administering a transdermal medication:

1. Assess the client to determine if the drug is safe and appropriate to give.
2. Check the medication, dose, volume, and expiration date.
3. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
    - During medication reconciliation
    - When preparing the medication
    - At the bedside
4. Wait to open the patch or disk until at the client's bedside.
5. Perform hand hygiene.
6. Don clean gloves for the administration of any patch or ointment. Never apply a patch or ointment with the bare hand because the medication can be transferred to you in the process.
7. Identify the client and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the blister pack, tube, or package, using the protocol recommended by the institution.)
8. Perform the third medication check at the bedside.
9. Explain the medication to the client:
    - Name (brand and generic)
    - Dosage
    - Indication, rationale, or reason for the drug to be given
    - Frequency
    - Route
    - Adverse effects
10. Remove any old patches that remain on the skin.
    - Many patches are small, clear, transparent disks, so some are difficult to find.
    - Assess the skin for irritation at the site of the old patch.
11. Cleanse the skin with soap and water and allow it to dry before applying patches or ointments.
12. Ensure that the site of the new patch is free of irritation, scrapes, open sores, or bruises. It is best if it is located on an area with little to no hair.
13. Rotate sites each time a new patch is placed.
14. Label the patch prior to placing it on the client with the nurse's initials, the date, and the time administered.

15. Perform hand hygiene.
16. Document in the MAR.
17. Evaluate the client's response to the drug(s) within the appropriate time frame.

Nursing Implications for Transdermal Administration

The nurse should do the following for clients receiving a transdermal patch:

- Educate the client to administer the patch at the same time each day.
- Administer after a shower or bath.
- Always remain with the client until all medications are taken; do not leave drugs at the bedside unattended.
- Educate the client to develop a schedule for rotating the sites of application.
- *Never* cut a patch in half (unless allowed per the drug product's labeling) because this may release all of the medication at once, resulting in an overdose. Patches are developed with special technology to release the medication slowly over a long period of time. Some patches may only need to be replaced once each week.
- Don gloves to remove a patch and dispose of according to institutional policy. *Never* dispose of a patch in the trash. Children have removed them from the trash thinking they were stickers, and this resulted in harm to the child. Pets also have eaten them.
- Educate the client that the patch's effects may last for many hours following its removal (up to 72 hours).

Cutaneous Administration

Ointments and lotions are medications that can be applied to the skin. Some are used for local therapy (e.g., hydrocortisone lotion applied to a rash), whereas some are used for systemic absorption. A common medication that is delivered via an ointment for systemic absorption is nitroglycerin (for angina). This medication will be discussed specifically due to its unique formulation.

Steps to administering nitroglycerin ointment (nitroglycerin paste):

1. Assemble the appropriate equipment:
    - Gloves
    - Nitroglycerin ointment and application paper
    - Paper tape
2. Assess the client to determine if the drug is safe and appropriate to give.
3. Check the medication, dose, volume, and expiration date.
4. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
    - During medication reconciliation
    - When measuring the medication
    - At the bedside
5. Perform hand hygiene.
6. It is important to don clean gloves for the administration of ointment. Never apply ointment with bare hands because the medication can be transferred to you in the process.
7. Identify the client and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the tube of ointment, using the protocol recommended by the institution.)
8. Perform the third medication check at the bedside.
9. Explain the medication to the client:
    - Name (brand and generic)
    - Dosage
    - Indication, rationale, or reason for the drug to be given
    - Frequency
    - Route
    - Adverse effects
10. Remove any old nitroglycerin doses that remain on the skin.
    - Assess the skin for irritation at the site of the old nitroglycerin applicator paper.
11. Cleanse the skin with soap and water and allow it to dry before applying the ointment.

12. Ensure that the site of the new dose is free of irritation, open sores, scrapes, or bruises. It is best if it is located on an area with little to no hair.
13. Rotate sites each time ointment is applied.
14. To administer the drug, lay the applicator paper down on the counter with the print side facing down.
15. Measure the amount of ointment to be used on the applicator paper, which is marked in a 2-inch strip with marks every half inch. The ointment is in a tube similar to that of toothpaste and should be gently squeezed so that a strip of ointment is placed on the applicator paper in the appropriate measurement. For example, the provider may order "nitroglycerin ointment 1 inch every 6 hours." So, a one-inch ribbon of ointment would then be placed on the paper (see Figure 2.13).

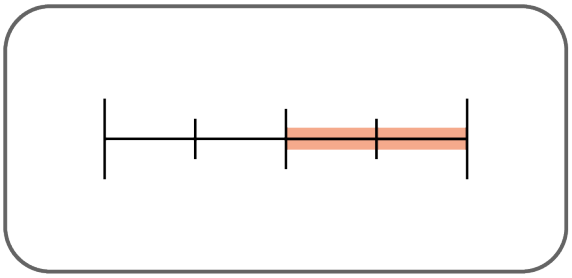


FIGURE 2.13 Nitroglycerin ointment is drawn up for administration on applicator paper. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

16. Apply the applicator paper with the ointment side closest to the skin.
17. Tape in place using nonallergenic tape. Plastic wrap may be taped over the applicator paper to protect clothes.
18. Label the applicator paper if this was not done prior to placing it on the client with the nurse's initials, the date, and the time administered.
19. Remove gloves and perform hand hygiene.
20. Document in the medication administration record.
21. Evaluate the client's response to the drug(s) within the appropriate time frame.

Nursing Implications for Cutaneous Application

The nurse should do the following for clients who are taking a **cutaneous** medication:

- Administer after a shower or bath.
- Educate the client to develop a schedule for rotating the sites of the application.
- Do not rub the ointment into the skin.
- For nitroglycerin ointment: Allow a nitro-free time period every 24 hours (this is usually done at night). Some providers will order "nitroglycerin ointment 1 inch every 6 hours. Take off at 10 p.m. Reapply at 6 a.m."
- As with transdermal patches, it is important to dispose of old ointment in a container safe from children or pets. A large dose of the medication will remain in the ointment, which may be toxic to children or pets.

Vaginal Administration

Vaginal medications may come in a variety of forms: creams, suppositories, foams, and so forth. Although vaginal suppositories may be inserted with a gloved finger, foams, creams, tablets, and jellies should be inserted with a special vaginal applicator. Table 2.8 lists the advantages and disadvantages of vaginal administration.

Advantages	Disadvantages
• Client can self-administer • Has local effects • Avoids first-pass effect	• Uncomfortable • Messy • May be irritating • Inconvenient for the client to use

TABLE 2.8 **Advantages and Disadvantages of Vaginal Administration**

Steps to administering vaginal medications:

1. Assemble the appropriate equipment
    - Clean gloves
    - Water-soluble lubricant for vaginal suppositories

- Vaginal applicator
- Perineal pad
- Medication

2. Assess the client to determine if the drug is safe and appropriate to give.
3. Check the medication, dose, and expiration date.
4. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
   - During medication reconciliation
   - When preparing the medication
   - At the bedside
5. Perform hand hygiene.
6. Don clean gloves for the administration of vaginal suppositories.
7. Request that the client void prior to inserting the medication.
8. Identify the client and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the blister pack, container, tube, or package, using the protocol recommended by the institution.)
9. Perform the third medication check at the bedside.
10. Explain the medication to the client:
    - Name (brand and generic)
    - Dosage
    - Indication, rationale, or reason for the drug to be given
    - Frequency
    - Route
    - Adverse effects
11. Provide privacy and drape the client with a sheet.
12. Position the client supine, hips elevated, knees bent, with the feet flat on the bed near the hips.
13. Provide perineal care as necessary.
14. Fill the applicator with the prescribed medication.
15. Lubricate with water-soluble lubricant.
16. Spread the labia, using the nondominant hand, and expose the vagina. Gently insert the applicator into the vagina approximately 2 inches using the dominant hand.
17. Push the plunger to deposit the medication into the vagina.
18. Remove the applicator and wrap it in a paper towel for cleaning later or disposal.
19. For suppositories, remove the wrapping and lubricate the room-temperature suppository with water-soluble jelly. Use an applicator if available; otherwise, use a finger on the dominant hand to insert the suppository about 3–4 inches into the vagina along its posterior wall. For creams or foams, insert 2–3 inches.
20. Client should remain in position for 10 minutes.
21. Apply a perineal pad if the client wishes.
22. Wash the applicator after each use.
23. Remove gloves.
24. Perform hand hygiene.
25. Document in the medication administration record.
26. Evaluate the client's response to the drug(s) within the appropriate time frame.

Nursing Implications for Vaginal Applications

The nurse should do the following for clients who are taking vaginal medications:

- Administer at bedtime, when possible, to allow the medication to remain in place for as long as possible.
- Assess for vaginal discharge and any other symptoms.
- Be clear in your teaching of the process because vaginal medications may be administered by the client.
- Educate the client to refrain from using douches and abstain from sexual intercourse after inserting medication.

Rectal Administration

Several medications can be given via the rectal route. This route can be used if clients are suffering from nausea and vomiting, especially if no IV is in place. This route has both a mixed first-pass effect and a non-first-pass effect. There are capillaries in the rectum that feed the portal circulation, which causes some of the medication to undergo first-pass effect; however, some of the medication will also be absorbed into the perirectal tissues locally.

Suppositories are medications that are solid at room temperature but soften and dissolve once in the rectal cavity. These medications are wrapped in foil or plastic packaging (see Figure 2.14), and it is important to remove the packaging prior to inserting the suppository in the client.

Table 2.9 lists the advantages and disadvantages of rectal administration.

Advantages	Disadvantages
• Very helpful for clients who are actively vomiting • Absorption is fairly rapid	• Partially undergoes first-pass effect • Absorption is very erratic and difficult to predict • Cannot be used in clients with recent prostate or rectal surgery or rectal trauma • Cannot be used in clients with rectal bleeding or diarrhea • Inconvenient for the client to use • Uncomfortable for the client

TABLE 2.9 Advantages and Disadvantages of Rectal Administration

Steps to administering rectal suppositories:

1. Assemble the appropriate equipment:
   - Gloves
   - Water-soluble lubricant
   - Medication
   - Bedpan, if client is on bed rest
2. Assess the client to determine if the drug is safe and appropriate to give. Assess for rectal bleeding or diarrhea.
3. Check the medication, dose, volume, and expiration date.
4. Follow the seven rights of medication administration *throughout* the procedure (at least three times or according to institutional policy).
   - During medication reconciliation
   - When preparing the medication
   - At the bedside
5. Perform hand hygiene.
6. Don clean gloves for the administration of rectal suppositories. Never apply with a bare hand.
7. Identify the client and verify allergies and reaction. (If the institution uses barcode scanning, scan the client's ID band and the barcode on the package using the protocol recommended by the institution.)
8. Perform the third medication check at the bedside.
9. Explain the medication to the client:
   - Name (brand and generic)
   - Dosage
   - Indication, rationale, or reason for the drug to be given
   - Frequency
   - Route
   - Adverse effects
10. Position the client on their left side with the uppermost leg flexed toward the waist. (This position is called the Sim's position or left lateral position.)
11. Provide privacy. Drape the client with a sheet.
12. Remove the foil or plastic wrapping from the medication (see Figure 2.14).

FIGURE 2.14 Suppositories, like the ones shown here, need to be removed from the wrapping before inserting in the client's rectum. (credit: "Suppositories in blister and one without packaging on white background (https://openstax.org/r/suppositories)" by Marco Verch/ Flickr, CC BY 2.0)

13. Lubricate the suppository with the water-soluble gel. Consider lubricating your gloved finger to support the client's comfort during this process. Never use petroleum-based products for lubrication because this may affect the absorption of the medication.
14. The suppository is usually shaped similarly to a bullet. Insert the rounded end into the rectum while instructing the client to take a deep breath and then exhale.
15. Insert the suppository along the side of the rectal wall, at least 1 inch beyond the internal rectal sphincter.
16. Instruct the client to remain on their left side for approximately 20 minutes to allow the suppository to be absorbed. If the medication is being given to stimulate defecation, it may take 20–30 minutes for that to occur. If the medication is given for other reasons, such as fever or nausea, it may take as long as an hour. Check the pharmaceutical information for specifics.
17. Remove gloves and perform hand hygiene.
18. Document in the medication administration record.
19. Evaluate the client's response to the drug(s) within the appropriate time frame.

Nursing Implications for Rectal Administration

The nurse should do the following for clients who are taking drugs rectally:

- Do not insert a rectal suppository into stool. Palpate the rectal wall for the presence of feces.
- Have the client defecate prior to inserting the suppository, if possible.
- Never divide suppositories.
- Loss of sphincter control may be seen in older clients. Have a bedpan handy.
- Suppositories may be administered by the client. Be clear in your teaching of the process.
- It is important to educate clients who are self-administering suppositories that these drugs are to be given rectally, not orally.

2.4 Dosage Calculations

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 2.4.1 Explain systems of measurement and conversion factors.
- 2.4.2 Interpret drug labels.
- 2.4.3 Correctly calculate drug dosages for administration.

Dosage calculations are an important part of drug administration, and the safety of the client depends on the nurse's ability to correctly calculate the dosage needed at any point in time. Drugs are not always available in the exact dosage or units of measurement that the client needs or the provider ordered. Knowing how to accurately calculate the amount needed is vital for the safety of the client. This chapter will review the units of measure used in drug calculations, introduce drug labels and explain how to interpret them, and acquaint the learner with various methods for performing drug calculations. The basis for all drug calculations is a fundamental knowledge of math skills and problem-solving.

Systems of Measurement

There are several different systems of measurement. The apothecary system, the household system, and the metric system are three of the most common.

Apothecary System

One of the older systems of measurement is the apothecary system, and it has been used by apothecaries or pharmacists for the last couple of centuries. This system is very difficult to use, and the Joint Commission, the FDA, and the Institute of Safe Medication Practice (ISMP) have recommended that it be discontinued. It is now seldom used, and the metric system was adopted. The nurse will rarely see an apothecary measurement, but it is important to understand how to correctly adapt an order using the apothecary system to the metric system. This can be accomplished through collaboration with the pharmacist or by using a table of weights and measures. The units of measure in the apothecary system are grains, drams, scruples, and the minim; the values are sometimes expressed as Roman numerals (e.g., X, IV) instead of Arabic numbers (e.g., 1, 2, 3, 4). The nurse should be aware of this; however, it won't be a focus of this chapter.

Household System

The household system (also known as the customary system) includes units of measure such as tablespoons, teaspoons, pounds, and ounces. Unfortunately, there has been much confusion in using this system, which leads to dosing errors. Thus, it is no longer used. The ISMP has issued recommendations to avoid household measurements. For conversion equivalents, see Appendix C: Drug Conversion Tables.

Metric System

Three types of metric measures are commonly used: length, volume, and weight. This section will cover only volume and weight. It is important to understand that the units can be smaller or larger in relation to their metric measure. The basic units are multiplied or divided by multiples of 10, which increases the ease of use when converting from one unit of measure to another.

Volume measures a liquid and is commonly used in dosage calculation when measuring liquid drugs, in the reconstitution of drugs, or with intravenous therapy. The metric system defines volume in units of liters. Weight measures mass and is commonly used in dosage calculation when a particular drug is administered based on the client's weight. The metric system defines weight in units of grams. A few examples are listed in Table 2.10, followed by their abbreviations and their equivalent number of grams. (See also Appendix A: International System of Units.)

Kilo indicates a larger unit of measurement and equals 1000. *Milli* indicates a smaller unit of measurement and equals 1/1000. *Micro* is also a smaller measurement and equals 1/1,000,000. Conversion between metric system units routinely occurs when you are preparing to administer drugs to clients.

	Metric Prefix	Example for Weight (abbreviation)	Conversion to Base Unit
Weight	Kilo	Kilogram (kg)	1 kg = 1000 g
	Base unit	Gram (g)	NA
	Milli	Milligram (mg)	1000 mg = 1 g
	Micro	Microgram (mcg)	1,000,000 mcg = 1 g
Volume	Base unit	Liter (L)	NA
	Deci	Deciliter	10 dL = 1 L

TABLE 2.10 **Common Metric Prefixes, Abbreviations, and Conversions Used in Dosage Calculation**

	Metric Prefix	Example for Weight (abbreviation)	Conversion to Base Unit
	Milli	Milliliter (mL)	1000 mL = 1 L
	Micro	Microliter (mcL)	1,000,000 mcL = 1 L

TABLE 2.10 **Common Metric Prefixes, Abbreviations, and Conversions Used in Dosage Calculation**

Note that the abbreviation for "micro" is sometimes shown as the Greek mu (μ, as in μg or μL); however, that practice is considered to be error prone by the Institute for Safe Medication Practices and has been supplanted by "mc," as in "mcg" for microgram or "mcL" for microliter.

PRACTICE PROBLEMS

Metric: Levels of Measurement

Determine the missing value.

1. 1000 g = _____ kg
2. 1000 mcg = _____ mg
3. 1000 mL = _____ L
4. 1 mg = _____ mcg
5. _____ g = 1500 mg
6. _____ L = 2000 mL
7. 750 mg = _____ g
8. _____ mg = 5000 mcg

Solutions:

1. 1 kg
2. 1 mg
3. 1 L
4. 1000 mcg
5. 1.5 g
6. 2 L
7. 0.75 g
8. 5 mg

PRACTICE PROBLEMS

Metric vs. Household Measurements

Calculate the missing value. Use the table in Appendix C: Drug Conversion Tables for household equivalents.

1. 2.2 lb = _____ kg
2. 10 ounces = _____ mL
3. 3 tsp = _____ mL
4. $\frac{1}{2}$ cup = _____ mL
5. _____ kg = 143 lb
6. _____ L = 4000 mL
7. 75 mg = _____ g
8. _____ mL = 4 Tbsp

Solutions:

1. 1 kg
2. 296 mL
3. 15 mL
4. 118 mL
5. 65 kg
6. 4 L

7. 0.075 g
8. 60 mL

Drug Labels and Precautions

To safely administer drugs to clients, one must understand the drug label and precautions listed. Components of a drug label (see Figure 2.15 and Figure 2.16) include drug generic and brand names, the strength of the drug, drug form, route of administration (if indicated), dosage and administration instructions, expiration date, controlled substance notification (if indicated), drug reconstitution (if indicated), and if the drug is a single or multidose vial (if indicated).

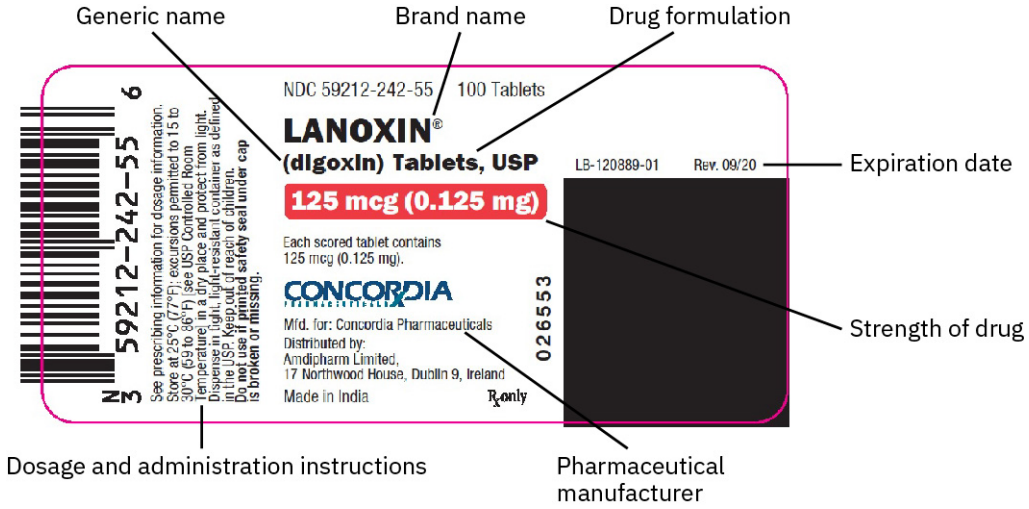


FIGURE 2.15 This image of a Lanoxin label depicts areas where drug label components are found. (credit: modification of work "LANOXIN-digoxin tablet" by National Library of Medicine/DAILYMED, Public Domain. Drug Company Logo All Rights Reserved.)

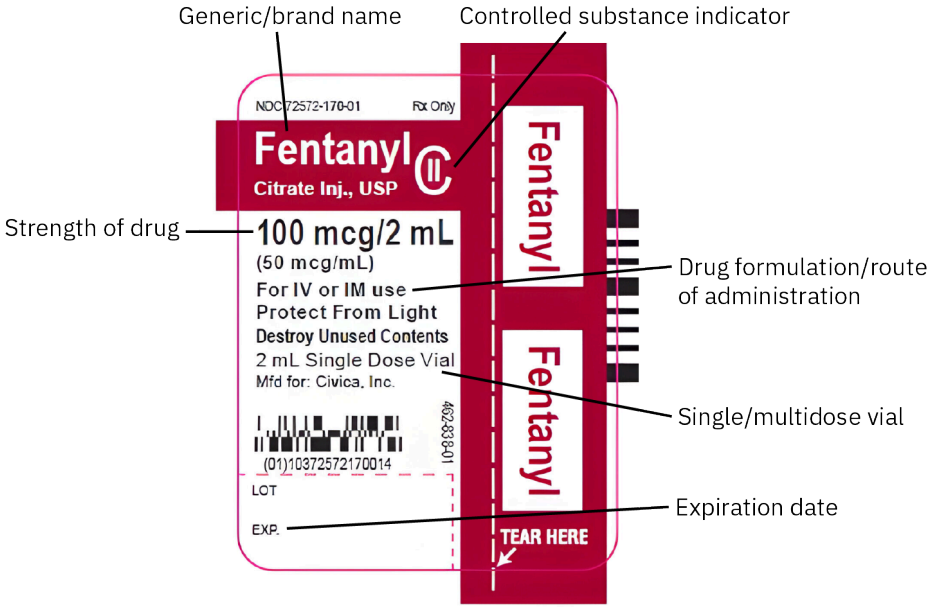


FIGURE 2.16 This Fentanyl label depicts areas where the drug label components are found for a controlled substance. (credit: modification of work "FENTANYL CITRATE injection" by National Library of Medicine/DAILYMED, Public Domain)

Drug Calculation Methods and Rounding Rules

There are three general methods for drug calculation: basic formula method, ratio and proportion, and dimensional analysis. It is recommended that the learner use the method they are most comfortable with. Additionally, some drugs require dosing based on weight and/or **body surface area**. These drugs require additional calculation.

Basic Formula Method

The basic formula method, also known as Desire Over Have, is the simplest of the drug calculation methods.

$$\frac{D}{H} \times Q = X$$

D = Desired dose (the dose ordered)
H = Amount on hand or available
Q = Quantity or volume of the drug form (tablet, capsule, liquid)
X = Amount calculated to be administered to the client

To use this method:

1. Write the desired dose or the dose ordered.
2. Write the drug dose on hand (available).
3. Divide the desired dose by the dose on hand and multiply by the quantity or volume of the drug form to get the amount calculated to be administered to the client.

Note: It is extremely important that the units of measure are the same when doing these calculations. If the desired dose is in mg, the on-hand amount must also be in mg. The amount to be administered will be in the same units as the quantity or volume of the drug form.

Example:

Desired dose: Lisinopril 10 mg orally BID (twice a day)
On hand: Lisinopril 2.5 mg per 1 tablet
How many tablets should the client receive per dose?

D = Desired dose (order) = 10 mg
H = Drug on hand (what is available) = 2.5 mg per 1 tablet
Q = 1 tablet

$$\frac{10 \text{ mg}}{2.5 \text{ mg}} \times 1 \text{ tablet} = 4 \text{ tablets}$$

10 mg divided by 2.5 mg = 4
4 × 1 tablet = 4 tablets

The amount to be administered to the client is 4 tablets.

PRACTICE PROBLEMS

Basic Formula Calculations

Solve for the dosage (X).

1. *Ordered:* Amoxicillin suspension 250 mg orally BID
   Available: Amoxicillin suspension 125 mg in 5 mL
   $\frac{250 \text{ mg}}{125 \text{ mg}} \times 5 \text{ mL} = X \text{ mL}$
2. *Ordered:* Potassium chloride orally 40 mEq BID
   Available: Potassium chloride elixir 20 mEq per 15 mL
   $\frac{40 \text{ mEq}}{20 \text{ mEq}} \times 15 \text{ mL} = X \text{ mL}$
3. *Ordered:* Furosemide 60 mg IVP (intravenous push) now
   Available: Furosemide 20 mg in 2 mL
   $\frac{60 \text{ mg}}{20 \text{ mg}} \times 2 \text{ mL} = X \text{ mL}$

Solutions:

1. 10 mL

2. 30 mL
3. 6 mL

LINK TO LEARNING

Formula Method Calculations

Access multimedia content (https://openstax.org/books/pharmacology/pages/2-4-dosage-calculations)
Understanding how to properly calculate dosage is important for nurses. This video provides additional information on the Formula or Desired Over Have method of dosage calculations.

Ratio and Proportion Method

The ratio and proportion method uses a linear equation to solve the dosage calculation problem.

K = Known dose (available)
M = Known unit of measure
D = Desired/ordered dose
X = Desired amount to be administered

$$K \text{ (known dose)} : M \text{ (known unit of measure)} = D \text{ (desired or ordered dose)} : X \text{ (desired amount)}$$

To use this method:

1. Write the known dose (dosage strength from drug label). (See *K* in the above formula.)
2. Write the known unit of measurement (also found on the drug label). (See *M* in the above formula.)
3. Write the desired ordered dose (usually found in the physician's orders). (See *D* in the above formula.)
4. Write *X* in the above formula as the placeholder for the desired amount to be administered. You will solve for *X*.
5. Check the units of measurement to make sure they are the same (e.g., mg : mg or tablets : tablets). Note that if they are not the same, you must convert them to the same unit of measurement prior to solving for *X*.
6. Solve for *X* (the desired amount to be administered to the client) by multiplying the means (*M* and *D* in the middle of the formula above) and the extremes (*K* and *X* on the outside of the formula). (Work only with the numbers and not the units of measurement.) Clear the *X* by dividing both sides of the equation by the number in front of the *X*, which solves *X*.

Another method of setting up a ratio and proportion equation is as follows:

$$\frac{K \text{ (Known dose)}}{M \text{ (Known unit of measure)}} = \frac{D \text{ (Desired/ordered dose)}}{X \text{ (Desired amount to be administered)}}$$

To solve this type of equation, cross multiply: $(KX) = (MD)$. (Work only with the numbers and not the units of measurement.). Clear the *X* by dividing both sides of the equation by the number in front of the *X*, which solves for *X*.

Example:

Ordered: Lisinopril 10 mg orally BID
Available: Lisinopril 2.5 mg
How many tablets should the client receive per dose?

$K : M = D : X$	$\frac{K}{M} = \frac{D}{X}$
2.5 mg : 1 tablet = 10 mg : *X* tablets	2.5 mg : *X* tablets = 1 tablet : 10 mg
$2.5X = 1 \times 10$	$2.5X = 1 \times 10$
X = 4 tablets	X = 4 tablets

FIGURE 2.17 These formulas show two different ways to solve the example problem using the ratio and proportion method. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

PRACTICE PROBLEMS

Ratio and Proportion Calculations

Solve for the dosage (*X*).

1. *Ordered:* Amoxicillin suspension 250 mg orally BID
   Available: Amoxicillin suspension 125 mg in 5 mL
   $$125\,\text{mg} : 5\,\text{mL} = 250\,\text{mg} : X\,\text{mL}$$
   $$125X = 250 \times 5$$
   $$X = \text{How many mL?}$$
2. *Ordered:* Potassium chloride PO 40 mEq BID
   Available: Potassium chloride elixir 20 mEq per 15 mL
   $$20\,\text{mEq} : 15\,\text{mL} = 40\,\text{mEq} : X\,\text{mL}$$
   $$20X = 40 \times 15$$
   $$X = \text{How many mL?}$$
3. *Ordered:* Furosemide 60 mg IVP now
   Available: Furosemide 20 mg in 2 mL
   If solving by cross multiplying, using $\frac{K}{M} = \frac{D}{X}$:
   $$20\,\text{mg} : 2\,\text{mL} = 60\,\text{mg} : X\,\text{mL}$$
   $$20X = 60 \times 2$$
   $$X = \text{How many mL?}$$

Solutions:

1. 10 mL
2. 30 mL
3. 6 mL

Dimensional Analysis Method

Dimensional analysis is one of several methods for determining the correct dose of medication. Dimensional analysis uses a series of equivalent measurements to change one unit of measurement to another to solve a problem. This method uses equivalent measurements that are set up as a series of "fractions," called conversion factors (or dimensions), that are used to cancel unnecessary units of measurements, leaving only the desired answer. There are times when there will be a number on top but not on the bottom. (These are not true fractions.)

To use this method:

1. Determine what you want to find (or solve for). Consider this a road map to your destination—where you want to go. Place the units of measure or quantity you want to find on the *right* side of the equation following the equal sign.
2. Typically, you will then start on the far left with the provider's medication order. Once you know what you wish to find (the provider's order), place that number and unit at the *top left* portion of the equation.
3. Use the information provided to slowly move forward, canceling units of measure when possible and circling units of measure you are looking for (using the road map as a guide).

In the first example below:

1. *X* number of tablets are placed on the right side of the equation following the equal sign because you are solving for how many tablets should be given.
2. 10 mg is placed in the upper left side in the numerator position.
3. Because you are solving for the correct number of tablets, tablet must be on the top left of the equation and not canceled out. And because mg is not on the right side of the equation, mg should be canceled out. That helps determine the placement of the next part of the equation.
4. One tablet must be on top so that the mg in 2.5 mg can be canceled out.
   $$OA \times DS = DA$$

OA = Ordered amount (or desired dose)
DS = Dosage strength
DA = Desired amount

Example 1:
Ordered: Lisinopril 10 mg PO BID
Available: Lisinopril 2.5 mg

How many tablets should the client receive per dose?

$$OA \times DS = DA$$

1. First, determine what goes on the right side of the equation. What units of measure are you solving for? In this example, it is tablets.
2. Then, identify the information on the top left—in this example, 10 mg have been ordered. Note that there is no number or letter under the 10 mg; leave it blank.
3. Cross out the units of measure—mg (numerator) and mg (denominator).
4. Now solve the math: $10 \text{ mg} \times 1 = 10$. Divide by 2.5 and solve for *X* (see Figure 2.18).

$$\frac{10 \text{ mg}}{\square} \times \frac{1 \text{ tablet}}{2.5 \text{ mg}} = \frac{10}{2.5} = X \text{ tablets}$$

$$X = 4 \text{ tablets}$$

FIGURE 2.18 This equation demonstrates dimensional analysis for solving the number of tablets that the client should be given. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Example 2:
Ordered: Give digoxin 0.5 mg IV push × 1 dose now
Available: Digoxin 0.25 mg/1 mL

How many mL should be given?

1. First, determine what goes on the right side of the equation. What units of measure are you solving for? In this example, it is mL.
2. The next step is to identify the information on the top left of the equation, which is the ordered amount of 0.5 mg. Note that there is nothing under 0.5 mg. Leave it blank.
3. Cross out the units of measure—mg (numerator) and mg (denominator).
4. Now solve the math: $0.5 \text{ mg} \times 1 = 0.5$. Divide by 0.25.
5. The answer is 2 mL (see Figure 2.19).

$$\frac{0.5 \text{ mg}}{\square} \times \frac{1 \text{ mL}}{0.25 \text{ mg}} = 2 \text{ mL}$$

FIGURE 2.19 This example of dimensional analysis is for an IV push medication. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Dimensional analysis is particularly helpful for more complicated equations, such as the following one. Note how the information can unfold as you add units of measure and cancel out as needed.

Example 3:
Ordered: Initiate dopamine IV infusion at 5 mcg/kg/minute
Available: Dopamine hydrochloride 800 mg in 500 mL normal saline
Client's weight: 176 lb

How many mL/hour should the medication infuse?

1. First, determine what goes on the right side of the equation. What units of measure are you solving for? In this example, it is mL/hour.
2. Now identify the information on the top left of the equation. In this example, it is 5 mcg. The order reads 5 mcg/kg/min. Therefore, 5 mcg goes on the top left, and kg/min is on the bottom left.
3. To solve the equation, the client's weight of 176 lb will also need to be converted within the equation. The following shows how the equation for solving for this infusion rate should be laid out. (It does not have to be

laid out in this specific order, but all units of measurement should be included; for example, 1 kg/2.2 lb could switch places with 500 mL/800 mg).

$$\frac{5 \text{ mcg}}{\text{kg/min}} \times \frac{1 \text{ kg}}{2.2 \text{ lb}} \times \frac{176 \text{ lb}}{} \times \frac{60 \text{ min}}{1 \text{ hour}} \times \frac{1 \text{ mg}}{1000 \text{ mcg}} \times \frac{500 \text{ mL}}{800 \text{ mg}} = X \text{ mL/hour}$$

4. Because you are solving for mL/hour, circle mL on top and hour on the bottom, ensuring that those units of measure will not be crossed out.
5. To solve the problem, you need to cross out duplicate units of measure. For this equation you would cross out (a) mcg, (b) kg, (c) min, (d) lb, and (e) mg.
6. This leaves the desired measurement as mL/hour (see Figure 2.20).

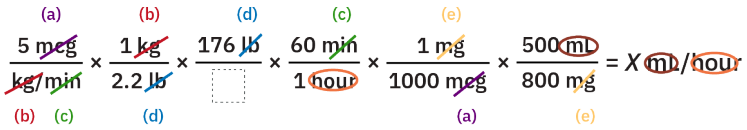


FIGURE 2.20 This shows the equation with the units of measure crossed out and the desired units of measure circled. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

7. Then multiply the numerators (top numbers) and multiply the denominators (bottom numbers) (see Figure 2.21).

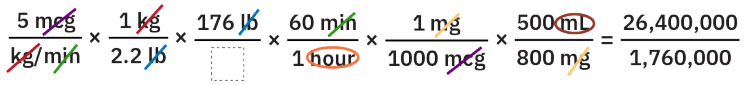


FIGURE 2.21 This stage of dimensional analysis shows the multiplication of numerators and denominators. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

8. You are now ready to solve for *X* by dividing the numerator of 26,400,000 by the denominator of 1,760,000.

$$\frac{26{,}400{,}000}{1{,}760{,}000} = X \text{ mL/hour}$$

$$X = 15 \text{ mL/hour}$$

PRACTICE PROBLEMS

Dimensional Analysis Calculations

Solve for the dosage (*X*).

1. *Ordered:* Omnicef 500 mg orally daily
   Available: Omnicef suspension 125 mg in 5 mL
   How many mL will be given?
   $$\frac{500 \text{ mg}}{} \times \frac{5 \text{ mL}}{125 \text{ mg}} = X \text{ mL}$$
2. *Ordered:* Zoloft 50 mg orally daily
   Available: Zoloft 25 mg tablets
   How many tablets will be given?
   $$\frac{50 \text{ mg}}{} \times \frac{1 \text{ tablet}}{25 \text{ mg}} = X \text{ tablets}$$
3. *Ordered:* Dopamine infusion at 3 mcg/kg/min
   Available: Dopamine 800 mg in 500 mL normal saline
   Client's weight: 86 kg
   At how many mL/hour will the infusion pump be set (round to the hundredth)? Hint: Use the template above, but because the client's weight is already listed in kilograms, there is no need to convert from pounds.
   $$\frac{2.5 \text{ mcg}}{\text{kg/min}} \times \frac{85 \text{ kg}}{} \times \frac{60 \text{ min}}{1 \text{ hour}} \times \frac{1 \text{ mg}}{1000 \text{ mcg}} \times \frac{500 \text{ mL}}{800 \text{ mg}} = X \text{ mL/hour}$$

Solutions:

1. 20 mL
2. 2 tablets
3. 7.97 mL/hour

LINK TO LEARNING

Dimensional Analysis Dosage Calculations

Access multimedia content (https://openstax.org/books/pharmacology/pages/2-4-dosage-calculations)
The dimensional analysis method can sometimes be complicated. This video provides additional information on performing dimensional analysis dosage calculations.

Body Weight Method

The body weight method allows dosage calculation for individualization. This method is commonly seen with medications with a narrow therapeutic index, drugs being adjusted due to the individual's ability to metabolize the drug, and pediatric clients.

$$\text{Drug dose} \times \text{Body weight} = \text{Client dose}$$

To use this method:

1. Convert the client's weight from pounds to kilograms $(2.2\ \text{lb} = 1\ \text{kg})$.
2. Determine the drug dose for body weight by multiplying them together.
3. Use your preferred dosage calculation method (formula, ratio proportion, or dimensional analysis) to solve for the dose of the drug to be administered to the client.

Example:
Ordered: Amoxicillin 10 mg per kg orally QID (four times a day)
Available: Amoxicillin 125 mg/5 mL
Client's weight: 110 lb

How many mL should the client receive per dose?

$$\frac{110\ \text{lb}}{2.2\ \text{kg}} = 50\ \text{kg}$$

$$10\ \text{mg (drug dose)} \times 50\ \text{kg} = 500\ \text{mg per dose}$$

Use the label shown in Figure 2.22 to calculate the number of mL per dose.

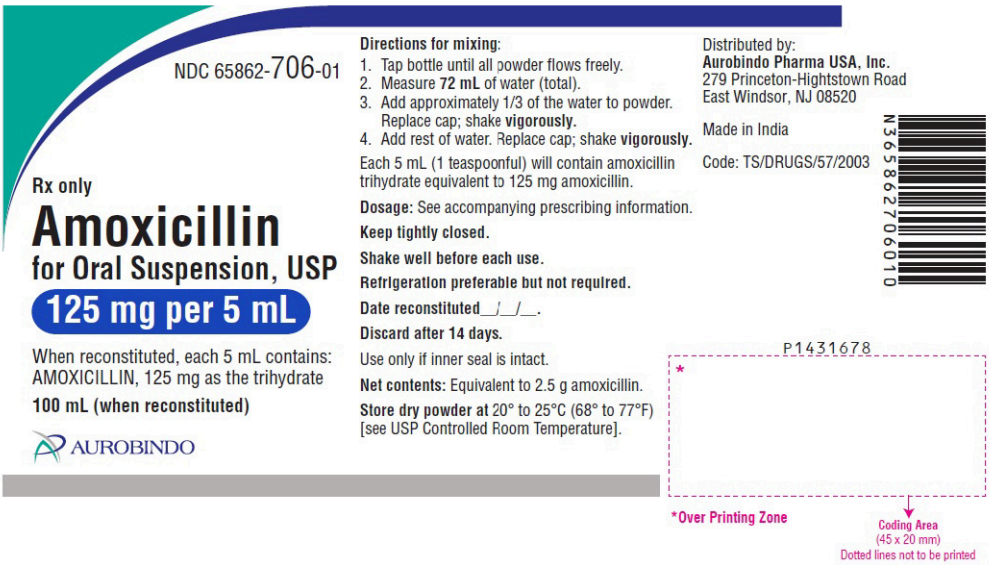


FIGURE 2.22 Use this label to calculate the desired dose using dimensional analysis. (credit: "AMOXICILLIN powder, for suspension, for suspension"by National Library of Medicine/DAILYMED, Public Domain. Drug Company Logo All Rights Reserved.)

Using dimensional analysis, it would look like this:

$$\frac{500\ \text{mg}}{1} \times \frac{5\ \text{mL}}{125\ \text{mg}} = 20\ \text{mL}$$

Body Surface Area Method

The body surface area (BSA) method allows dosage calculation for individualization. This method is commonly seen with medications that have a narrow therapeutic index, drugs that are being adjusted due to the individual's ability to metabolize the drug, chemotherapeutic agents, pediatric clients, and clients with burns. It is an approximation of the total skin area of an individual measured in meters squared (m^2). BSA is calculated using the square root calculation as determined by the client's height and weight.

To use this method:

1. Convert pounds to kilograms.
2. Calculate BSA. The formula is:
$$\sqrt{\frac{[\text{height (cm)} \times \text{weight (kg)}]}{3600}}$$
3. Calculate the dose in mg.
4. Calculate the dose in mL.

Example:

Calculate the dose of ceftriaxone in mL for a client who weighs 37 lb and is 97 cm tall. The dosing required is 2 mg/m^2, and the drug comes in 1 mg/mL.

1. $37\ \text{lb} \div 2.2\ \text{kg} = 16.8\ \text{kg}$
2. $\sqrt{16.8\ \text{kg} \times 97\ \text{cm} \div 3600} = 0.67\ \text{m}^2$
3. $2\ \text{mg/m}^2 \times 0.67\ \text{m}^2 = 1.34\ \text{mg}$
4. $1.34\ \text{mg} \div 1\ \text{mg/mL} = 1.34\ \text{mL}$

The dose to be administered is 1.34 mL.

To calculate the dose using dimensional analysis, some of the same steps are used.

1. $37\ \text{lb} \div 2.2\ \text{kg} = 16.8\ \text{kg}$
2. $\sqrt{16.8\ \text{kg} \times 97\ \text{cm} \div 3600} = 0.67\ \text{m}^2$
3. $0.67\text{m}^2 \times 2\ \text{mg/m}^2 = 1.34\ \text{mL}$

Remember that body surface area is measured in meters squared (m^2). Begin the dosage calculation by calculating the body surface area of the client, then multiply the size of the client by the ordered dose to obtain the dose needed for the client.

$$\text{Client size} \times \text{Order} = \text{Dose}$$

CLINICAL TIP

Body Surface Area Calculator

BSA is estimated by using a formula; however, this can be simplified by using a BSA calculator (https://openstax.org/r/calcsurface).

Rounding Rules

Nurses must know when and how to round medication doses. Caplet and tablet doses can be rounded to the nearest half-tablet if they are scored. Some are scored in fourths and can be rounded accordingly. Caplets and tablets that are controlled release, extended release, sustained release, or enteric-coated should not be split or crushed. Capsules are rounded to the nearest whole number because they cannot be divided. Liquid drugs are rounded to the nearest tenth. If the nurse is calculating a liquid medication for drops, then it is to be rounded to the nearest whole number because it is not possible to administer a partial drop. These rounding rules guidelines (https://openstax.org/r/safemedicate) assist the nurse with rounding medication doses. The National Library of Medicine (https://openstax.org/r/ncbinlmnih) provides another resource for rounding as well as performing calculations.

Next, rounding is determined by how many places from the decimal point are appropriate. If a number to the right of

the decimal point needs to be rounded and it is 4 or less, then it is rounded down. For example, if the nurse calculated that they were to give 1.243 and they were rounding to the nearest tenth, the number would be rounded to 1.2. If a number to the right of the decimal point is 5 or greater, then it should be rounded up. For example, if the nurse calculated that they were to give 1.251 and they were rounding to the nearest tenth, the number would be rounded to 1.3.

SAFETY ALERT

Rounding

The nurse must always guard against the possibility of an overdose of medication. When in the pediatric setting or when working with high-alert medications, rounding rules may change. Many institutions round down in the pediatric setting to prevent overdose. Sometimes the numbers after the decimal point are dropped so that 5.642 mL becomes 5 mL. This is known as rounding off or cutting off. It is imperative that the nurse be familiar with the policies of their institution. Most EMRs now have standardized rounding policies to assist the nurse.

Chapter Summary

This chapter described drug administration as it relates to the nursing process and nursing clinical judgment. The importance of client teaching during drug administration was explained, and the components of teaching and learning were discussed. The processes of pharmacokinetics and pharmacodynamics were clarified with the concepts of half-life, bioavailability, and therapeutic index. This chapter reviewed the different routes of medication administration and nursing interventions related to drug administration. The chapter finished with an explanation of drug calculations and a review of the systems of measurement.

Key Terms

absorption the transmission of a drug from the site of administration to the bloodstream

adverse drug reaction an undesirable, unexpected, and potentially dangerous response to a drug that occurs at therapeutic drug dosages

affinity the strength of attraction of a drug to a receptor site; drugs with high affinity have a strong attraction to the receptor

agonist a drug that interacts with a receptor, causing a response

antagonist a drug that blocks a receptor, thus blocking an agonist from binding to the receptor and activating it

bioavailability the drug concentration available to bind to receptors at its target tissue or site of action; a subcategory of absorption

body surface area the total surface area of the human body; to be used as a tool in the calculation of dosing medications

cutaneous relating to the skin

deltoid a muscular area located above the armpit and 2 to 3 fingerbreadths below the acromion process used for small intramuscular injections (less than 1 mL of medication)

dependence when the body has a physiological or psychological need for a drug

distribution the transportation of medication to the sites of action via bodily fluids; it is influenced by the ability to travel to the site of action through the bloodstream

duration of action the length of time that a drug's concentration is sufficient to cause a therapeutic response

enteral the administration of medication via the gastrointestinal (GI) tract

excretion the elimination of drugs from the body, primarily through the kidneys

first-pass effect a phenomenon in which an oral drug gets metabolized at a specific location in the body that results in a reduced concentration of the active drug upon reaching its site of action

half-life the time it takes for the serum drug concentration to be reduced by 50%

health literacy an individual's ability to obtain, understand, and make appropriate decisions based on information to promote their health and wellness

indication the reason why a drug might be given

intramuscular the administration of a drug into a muscle

intravenous (IV) the administration of a drug directly into a vein

intrinsic activity the maximal effect that can be produced by a drug

ligand a molecule that binds to a receiving protein molecule or receptor

mechanism of action the way a drug produces its effects on the body, or the way a drug works

medication reconciliation the process of identifying and verifying the most accurate list of medications that a client is taking, including the drug name, dosage, frequency, and route that the client is taking

metabolism where a drug is changed into a less active or an inactive form by the action of enzymes—usually in the liver—and then is excreted in the stool or urine; metabolism prepares a drug for excretion from the body

minimum effective concentration (MEC) the minimum concentration of a drug that produces an intended therapeutic effect

onset of action the time at which a drug produces a therapeutic effect after drug administration

parenteral the administration of medication anywhere other than the gastrointestinal (GI) tract

partial agonist drugs that function as either agonists or antagonists depending upon the level of the surrounding full agonist

peak the time during which a drug has the maximum serum concentration

pharmacodynamics the way a drug interacts with receptors, target cells, body systems, and organs to produce effects, or what the drug does to the body

pharmacokinetics the movement of a drug through the body, or what the body does to the drug

receptor a reactive site on the surface or inside of a cell; often what happens with a drug is that it attaches itself to a receptor to elicit a therapeutic

response

side effect secondary effects produced by a drug at therapeutic doses

subcutaneous the administration of a drug into the adipose (fat) tissue

therapeutic effectiveness the drug is doing what the drug is supposed to do—the most important quality a drug should have

therapeutic index the ratio of the dose of a drug that produces a therapeutic effect to the dose that causes toxicity; sometimes known as the therapeutic window

tolerance a condition where the body adapts to a substance (drug) after repeated administration, and gradually, over time, the body requires higher doses to achieve the same initial effect (often seen in opioid use)

toxicity excessive amounts of a serum drug level in the body, usually seen when the body's normal mechanism for metabolizing or excreting a drug is compromised

transdermal topical administration of a drug through a patch on the skin

ventrogluteal a muscular area below the iliac crest on the lateral aspect of the thigh considered to be the safest, most preferred site for intramuscular injections

Review Questions

1. The client is taking an 800 mg dose of a medication with a half-life of 4 hours. How much medication will be available in the body after 12 hours?

a. 400 mg
b. 200 mg
c. 100 mg
d. 50 mg

2. Which laboratory test should the nurse check prior to administering a drug that can cause harm to the kidneys?

a. Hemoglobin
b. Alanine transaminase
c. Aspartate transaminase
d. Serum creatinine

3. The nurse is preparing to administer an intramuscular injection in the deltoid muscle. At which site will the nurse inject the medication?

a. 1.5 inches below the acromion process
b. 1 inch in front of the acromion process
c. At the level of the axilla
d. Between the acromion process and the scapula

4. The nurse is teaching a client about self-administering a fentanyl transdermal patch. Which statement indicates an understanding of client teaching?

a. "I will cut the patch in half when my pain is not severe."
b. "I will rotate the patch application site every 7 days."
c. "I will remove the old patch before applying a new one."
d. "I will cleanse the application site with alcohol before applying."

5. Which action will the nurse take when administering a subcutaneous enoxaparin injection?

a. Administer the injection at a 90-degree angle.
b. Aspirate for blood return.
c. Administer the injection in the deltoid area.
d. Massage the site after injection.

6. When administering an oral medication to a client with renal insufficiency, which potential complication is of greatest concern to the nurse?

a. Decreased drug absorption

b. Increased risk of drug toxicity
c. Increased risk of an allergic reaction
d. Decreased therapeutic drug effects

7. When administering digoxin, a drug with a narrow therapeutic index, the nurse should assess for which effect?
a. Reduced first-pass effect
b. Increased tolerance
c. Reduced dependence
d. Increased toxicity

8. The health care provider has changed the order for a medication from an IV dose to an oral dose of the same medication. The oral medication has a high first-pass effect through the liver. What does the nurse expect to see when checking the order for the oral medication to achieve similar concentrations?
a. The oral medication dose will be the same as the IV dose.
b. The oral medication dose will be lower than the IV dose.
c. The oral medication dose will be higher than the IV dose.
d. The oral medication dose has no relation to the IV dose.

9. A client has been prescribed an oral medication that is supplied as a large unscored caplet. The client refuses to take the medication with the statement, "I cannot swallow such a large pill." What is the nurse's *best* action?
a. Convince the client to go ahead and take the medication.
b. Call the provider to request an IV form of the drug.
c. Break the caplet in half so it is easier to swallow.
d. Call the pharmacy and request an oral solution of the drug.

10. A client is complaining of severe pain and has an order for morphine sulfate. Which route would give the client the fastest pain relief?
a. PO
b. IV
c. IM
d. Subcutaneous

11. The provider has ordered dofetilide 0.5 mg orally every 12 hours. The pharmacy supplies dofetilide 125 mcg tablets. How many tablets will the nurse administer?
a. 0.5 tablets
b. 2 tablets
c. 3 tablets
d. 4 tablets

12. The provider has ordered meperidine 150 mg IM every 6 hours, as needed, for pain. The pharmacy supplies meperidine 100 mg/mL. How many mL should the nurse administer to the client?
a. 1 mL
b. 1.5 mL
c. 2 mL
d. 3.5 mL

13. The health care provider ordered heparin sodium 4000 units subcutaneously every 12 hours. The pharmacy supplies 5000 units/1 mL in a 10 mL vial. How many mL should the nurse administer to the client?
a. 0.8 mL
b. 1.2 mL
c. 8 mL

d. 2.5 mL

14. The health care provider ordered 10 mL of cough syrup for a client. How many teaspoons will the client take per dose?
a. 2
b. 5
c. 7.5
d. 10

15. The health care provider ordered enoxaparin 1.5 mg/kg/day. The client weighs 176 lb. How many milligrams of enoxaparin should the client receive?
a. 80 mg
b. 100 mg
c. 120 mg
d. 150 mg

16. The health care provider ordered 6 mg of dexamethasone sodium phosphate injection. The pharmacy provided a vial labeled 120 mg/30 mL. How many mL will be administered to the client? (Round to the nearest tenth.)
a. 0.6 mL
b. 1.5 mL
c. 2.3 mL
d. 3.3 mL

17. The provider ordered heparin sodium 1250 units/hour IV infusion. The pharmacy supplied heparin sodium 25,000 units in 500 mL of D_5W. Calculate the infusion rate in mL/hour.
a. 6 mL/hour
b. 12 mL/hour
c. 20 mL/hour
d. 25 mL/hour

18. The provider ordered fluoxetine hydrochloride 60 mg oral solution for a client who has difficulty swallowing. The pharmacy supplied fluoxetine hydrochloride oral solution 20 mg/5 mL in a 120 mL bottle. How many mL should the nurse administer?
a. 15 mL
b. 20 mL
c. 30 mL
d. 60 mL

19. The provider ordered moxifloxacin 400 mg IV piggyback daily. The pharmacy supplied moxifloxacin 400 mg in 250 mL normal saline. The instructions are to infuse over 60 minutes. At how many mL/hour will the infusion pump be set?
a. 100 mL/hour
b. 200 mL/hour
c. 250 mL/hour
d. 400 mL/hour

20. The provider ordered dobutamine hydrochloride 5 mcg/kg/minute IV for a 132 lb client. The pharmacy supplied 250 mg in 250 mL of D_5W. How many mL/hour should be infused?
a. 12 mL/hour
b. 15 mL/hour
c. 18 mL/hour
d. 23 mL/hour

CHAPTER 3

Ethics, Legal Considerations, and Safety

FIGURE 3.1 Pharmacology is the study of the biological effects of drugs on the body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The primary focus of this chapter is the quality of care and safety of the client as it relates to the administration of medications. The learner is introduced to legislative acts on a federal and state level that affect nursing. The emphasis then moves to client safety and the prevention of medication errors. The core ethical principles of nursing are discussed, and the learner is also introduced to the American Nurses Association (ANA) Code of Ethics. The chapter finishes with a discussion of nursing informatics and how it affects drug administration and error prevention.

3.1 Legal Considerations

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 3.1.1 Discuss federal legislative acts affecting nursing.
- 3.1.2 Describe the function of state nurse practice acts.

Federal Legislative Acts

Prior to 1906, there were no legal controls over the sale or quality of any drugs. Before this time, rattlesnake oil for pain and inflammation and other tonics could be sold out of the back of a covered wagon, a general store, or a doctor's office. There was nothing in place to protect the consumer from fraud or harm. The manufacturers were not required to list any of the ingredients in their elixirs, pills, or potions. It was not unusual for the medicine sold to ultimately cause harm rather than provide the cure that was advertised.

The Pure Food and Drug Act of 1906 controlled the manufacture, labeling, and sale of drugs. Although the law emphasized the importance of accurate labeling, it also prohibited certain ingredients from being used within drugs. It also prohibited contaminated or misbranded foods and drugs for either humans or animals from being sold across state lines (Petruzzello, 2023). It also established the National Formulary (NF) and the U.S. Pharmacopeia (USP) as the standards for such products. A brief description of important federal legislation is provided in Table 3.1.

Year	Law	Purpose
1906	Pure Food and Drug Act (also known as the Wiley Act)	• Initiated government regulation of interstate drug sales • Led to the creation of a government agency that would later become the Food and Drug Administration (FDA) • Focused on accurate product labeling
1912	Sherley Amendment to the Pure Food and Drug Act	• Prohibited drug labels from containing false or misleading information
1938	Food, Drug, and Cosmetic Act	• Addressed drug safety • Required drug manufacturers to test all drugs for harmful effects, though it did not mandate that drugs be effective • Required that labels indicate if a drug was habit-forming
1952	Durham-Humphrey Amendment to the Food, Drug, and Cosmetic Act	• Gave the FDA the power to distinguish between prescription and nonprescription drugs
1962	Kefauver-Harris Amendments to the Food, Drug, and Cosmetic Act	• For the first time, this act required drug manufacturers to release proof of a drug's effectiveness as well as its safety • Established new guidelines for reporting adverse effects and contraindications of drugs
1970	Controlled Substances Act	• Led to the establishment of the Drug Enforcement Administration (DEA) in 1973 • Delineated the controls for manufacturing, distributing, and prescribing habit-forming drugs • Established drug schedules and provided drug treatment programs for individuals with substance use disorders
1994	Dietary Supplement Health and Education Act	• Reclassified herbal medicines, vitamins, minerals, amino acids, and other chemicals used for health purposes as "dietary supplements"
2013	Drug Supply Chain Security Act	• Outlined steps to trace drug products at the package level to identify and trace certain prescription drugs distributed across the United States • Established national licensure standards for wholesale distributors

TABLE 3.1 **Summary of Federal Legislation Regarding the Safety of Medications in the United States**

Other important federal legislation impacting health care in the United States include the Health Insurance Portability and Accountability Act (HIPAA), the Health Information Technology for Economic and Clinical Health (HITECH) Act, and the **Affordable Care Act** (ACA).

Health Insurance Portability and Accountability Act (HIPAA)

The **Health Insurance Portability and Accountability Act** (HIPAA) was enacted by Congress in 1996. It is a federal law that set forth standards to protect sensitive health information from being divulged without the consent or knowledge of the client. Its purpose was to:

- Establish the Privacy Rule
- Establish the Security Rule for protecting electronic health information
- Ensure that covered entities report and resolve any breaches in security

This discussion will focus on the Privacy Rule, which protects a client's individually identifiable health information no matter what form the information is in—oral, written, or transmitted. The Privacy Rule designates this information as **protected health information (PHI)** and essentially covers any data by which the individual can be identified (name, date of birth, Social Security number, address, phone number, etc.) in relation to their health condition, provision of health care, or payment (past, present, and future) (U.S. Department of Health and Human Services, 2021). It allows PHI to be shared between health care providers and insurance companies to provide high-quality health care. Individual practitioners and health care institutions may have civil or criminal penalties levied against them for violation of the HIPAA Privacy Rule. Nurses should be alert to situations in which violations might occur, such as discussions in common areas where one might be overheard, inappropriate use of social media, or deliberate violations where one intentionally discloses personal information. In cases of deliberately violating the Privacy Rule, the penalties to the health care worker and the institution can be quite severe.

Each client has the right to **confidentiality** and to determine who has access to their PHI. Health care providers should not share confidential information obtained from the client with others without their express authorization. Once the nurse obtains the client's health information (biographical information, chief complaint, medical and surgical history, medications and allergies, family history, social history, signs and symptoms of present illness, and physical assessment), the nurse should ascertain how it is to be treated and who will be given access to it. Confidentiality should still be observed when obtaining a medication history because some medications will reveal the treatment of specific diseases; for example, if a client is taking carbidopa/levodopa, they likely have Parkinson's disease. However, an incorrect assumption could also be made. Aripiprazole (Abilify) is used for the treatment of psychosis; however, it also treats depression. The nurse should not assume that the client has schizophrenia or psychosis because they have been prescribed that drug. When reviewing medication information with the client, it is important to protect the client's privacy by providing a private area for the discussion. The U.S. Department of Health and Human Services provides more information about how HIPAA affects health care professionals (https://openstax.org/r/professionalsin).

TRENDING TODAY

Social Media

Social media is a powerful tool, and nurses can use this tool to inform the public about health, wellness, and illness. Nurses can also use social media to disseminate information, network, and educate others about important topics. However, it is crucial for nurses and others in the health care profession to be very mindful of the accuracy of the information they post, to exhibit professional behavior, and to maintain client confidentiality at all times, as this article from the *HIPAA Journal* (https://openstax.org/r/hipaajournalcomj) illustrates.

There are certain conditions under which PHI can be disclosed without the consent of the client. The information may be given to other providers who are treating the client, as well as insurance companies, but it also can be released if required by law or a court order for the intent of protecting public health or in cases of abuse or neglect.

CLINICAL TIP

HIPAA

Nurses should take HIPAA concerns very seriously. No PHI should be shared unless it is on a "need-to-know" basis. Information should be shared only in secure locations. Be alert to situations where information could be overheard unintentionally, such as in elevators or the cafeteria.

Health Information Technology for Economic and Clinical Health (HITECH) Act

The **Health Information Technology for Economic and Clinical Health (HITECH) Act** was enacted in 2009 to improve the efficiency and quality of care for clients through the adoption of electronic health records (EHRs) across

the United States. Prior to the adoption of the EHR, records were handwritten or typed notes by providers, which were then stored in paper files in a medical records department. The HITECH Act also had a meaningful use (MU) element whose purpose was to provide an incentive for institutions and providers to adopt the EHR. In the beginning, the Centers for Medicare and Medicaid Services (CMS) provided financial incentives to physicians, and then physicians proved MU by reporting clinical quality measures for the purpose of improving client outcomes (Brooks et al., 2022). CMS had several objectives for MU:

- Use of the EHR in a meaningful, significant way
- Advancing clinical processes to improve the quality of health care
- Improving client outcomes through the use of quality measures

In 2018, CMS renamed the Meaningful Use program to the Promoting Interoperability Program. This expanded the focus to the interoperability of EHRs with the goal of improving client access to health information, health information exchange among health care providers, and data collection.

Approximately 98% of hospitals have adopted some type of EHR, regardless of whether it would be described as basic or comprehensive (Apathy et al., 2021). The adoption of EHRs and the use of health information technology (HIT) has presented several challenges, including cost, usability, and a lack of interoperability. The Office of the National Coordinator for Health Information Technology is a U.S. government organization that has developed various strategies to assist with the burden related to HIT and to help agencies, institutions, and clinicians become more efficient through the use of technology.

The addition of the electronic medication administration record is an important component of the EHR, and many institutions now use e-prescriber or computerized prescriber order entry (CPOE). This is discussed more in the last section of this chapter.

The Affordable Care Act (ACA)

President Barack Obama signed the **Affordable Care Act** (ACA) into law in 2010. This law (sometimes called Obamacare) had three primary aims:

- Make health insurance available and affordable to more Americans
- Expand the Medicaid program by expanding the federal poverty level
- Support innovative medical care delivery methods with the objective of lowering health care costs (HealthCare.gov, n.d.)

The ACA prohibited insurance companies from charging excessive amounts for premiums and contained measures to ensure that the consumer received value for the cost of their premiums. It raised the age limit to 26 years of age for children to continue to be covered by a parent's insurance. It also allowed individuals with preexisting conditions to obtain and keep insurance coverage and provided preventive care. Under the ACA, there are medications with limited cost-sharing; these drugs are covered with little to no copay. Some of these medications include contraceptives, vaccines, aspirin, statins, tobacco cessation products, and breast cancer primary prevention drugs. This law was considered controversial when passed and has undergone several changes since 2010; however, many Americans consider the ACA positively (Kaiser Family Foundation [KFF], 2023). Although many more Americans are now insured, unfortunately, 27.5 million individuals in the United States still do not have insurance coverage (Tolbert et al., 2022).

State Nurse Practice Acts

All clients have the right to safe, competent nursing expertise. Each state and territory within the United States has legislated a nurse practice act (NPA) to create a board of nursing (BON). The focus of a BON is to protect and promote the welfare of the *public* across the state, and it is responsible for implementing and enforcing the NPA. It does so by ensuring that each person licensed to practice as a nurse is competent to practice. For an individual to become licensed, they must meet the minimum competencies set forth by each board. The NPA is a series of state statutes that contains the laws related to prospective nurses and the nurses' education, licensure, practice, and grounds for disciplinary actions.

Each BON sets the educational standards for all nursing programs across the state, which prepares individuals to become licensed registered nurses. This includes prelicensure programs as well as advanced practice. All applicants

must complete specific educational requirements, pass a national licensing exam (the National Council Licensure Examination [NCLEX]), and obtain clearance through a background check that looks for any criminal conviction that might make the applicant unfit for licensure. Criminal conviction may or may not disqualify an individual from being licensed as a nurse; most states decide on a case-by-case basis, depending on the crime. Some states require proof of continuing competency for licensure renewal. This might be in the form of a certain number of hours of continuing education in the area of the nurse's practice or a national nursing certification. There are many board-recognized credentialing agencies and providers.

LINK TO LEARNING

State Boards of Nursing

As mentioned above, each state and territory within the United States has legislated a nurse practice act to create a board of nursing or like entity. Find the board of nursing (https://openstax.org/r/rntravelwebco) for the state where you hope to practice after completing nursing training. Click on the individual state board of nursing site to familiarize yourself with the information available. Compare and contrast the different sites.

Most BONs were established about 100 years ago and have evolved over time. Many BONs have expanded their scope and now provide remediation for licensed nurses who have had some type of practice issue. The BON monitors compliance with the NPA and state laws. It is responsible for taking action against nurses who are unsafe or have engaged in professional misconduct.

State BONs often participate in multistate licensure compacts and may even act as a forum for individuals to report concerns about specific nursing services they have received. The states and territories that participate in these nurse licensure compacts allow a nurse to practice under a single license; for example, an individual holding a multistate license in Oklahoma is able to practice in Texas. Renewal and disciplinary actions are the responsibility of the state issuing the license (Oklahoma, in this case); however, the nurse is responsible for knowing and following the laws of the state in which they are practicing (Texas, in this example).

NPAs typically allow nursing students to practice nursing while under the auspices of an accredited nursing education program and under the supervision of qualified nursing faculty. Student nurses do *not* practice on a faculty member's license. Each nursing student is responsible for answering for any action they have taken and are held accountable to the same standards as a licensed nurse.

Strategies for Students in the Practice Setting

The nurse's primary responsibility is safe, effective care of the client. Understanding the expectations of faculty, the institution, and the BON is important for the nursing student. Some common guidelines for clinical practice that may be helpful to the student include:

- Providing safe, effective nursing care.
- Ensuring understanding of the educational program's and facility's policies before accepting any assignment.
- Demonstrating knowledge of the client's disease process, medications, nursing interventions, and plan of care.
- Informing the faculty when unprepared for an assignment.
- Seeking assistance if not prepared for a procedure (Callahan, 2023).
- Never practicing outside their scope of practice.
- Never going to a clinical site while impaired (this includes sleep deprivation).
- Being accountable for learning.
- Recognizing the limitations of their knowledge.

3.2 Drug Errors and Prevention

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 3.2.1 Define core ethical principles as they relate to drug administration.
- 3.2.2 Discuss ANA Code of Ethics principles related to safe drug administration.
- 3.2.3 Describe the benefit–risk ratio.
- 3.2.4 Identify steps to prevent medication errors.

Drug errors are a significant cause of morbidity and mortality in the United States. A medication error is "an error (of commission or omission) at any step along the pathway that begins when a clinician prescribes a medication and ends when the patient actually takes the drug" (Agency for Healthcare Research and Quality [AHRQ], 2019b, para. 1). This section addresses a nurse's response to medication errors, the role of prevention, and the ethics of dealing with an error once it happens.

Core Ethical Principles

According to Gallup's annual poll (Brenan, 2023), the American public ranked nurses number 1 (79%) as the most honest and ethical profession, above physicians (62%), high school teachers (53%), and pharmacists (58%). *Ethics* refers to the set of moral principles that direct how a person behaves. The foundations for an individual's ethical standards are one's values, or the personal beliefs someone has about what is right or wrong.

Integrity means doing the right thing—always—even when no one is looking. It means being truthful and having honor or strong moral principles. There are many components to having integrity in the life of a nurse. The nurse should check all actions, decisions, and planning ahead of time to ensure the "rightness" of an action or decision. Being honest and owning up to a medication error is not only "right" but also may save the life of the client if an intervention can prevent a bad outcome. One of the most important things an individual can say is, "I made a mistake, and this is what happened. What can we do to solve this problem?" The sooner a problem is recognized and brought to the attention of the charge nurse and provider, the more quickly a solution can be found.

Another crucial element to having integrity is owning the responsibilities that come with the job and being accountable for one's job performance. The nurse should take a moment to reflect on the day. Ethical care of the client is more than managing challenging decisions; it is about completing the mundane, day-to-day tasks to the best of one's abilities. Were the client and family truly cared for? Was the client's pain adequately controlled? Was teaching performed? Was the client adequately assessed prior to being given a drug? Was the nurse an advocate for the client? Was HIPAA violated in the elevator (or anywhere else)? Did the nurse demonstrate respect for the client? It is not unusual for ethical dilemmas to occur in the daily practice of nursing. Remembering the ethical principles of autonomy, beneficence, nonmaleficence, justice, veracity (truth), and confidentiality will provide a framework for the nurse as these conflicts arise.

Autonomy

Autonomy in medicine essentially means having the right to make one's own health care decisions, being independent, and having control over oneself. In the past, Western medicine operated under a paternalistic style of authority with a "doctor always knows best" philosophy. The physician guided the client's care, sometimes with little input from the client or family. In 1979, Beauchamp and Childress (2013) introduced the idea of autonomy as it related to biomedical ethics and identified that a client should be able to make uncoerced and informed decisions about their health.

A crucial piece of autonomy is having sufficient information to make a sound choice. Informed consent can assist the client in making appropriate choices for their body and deciding whether to pursue or decline specific medical treatments recommended by their provider. According to Varkey (2021, p. 19), "the requirements of an informed consent for a medical or surgical procedure, or for research, are that the client or subject (i) must be competent to understand and decide, (ii) receives a full disclosure, (iii) comprehends the disclosure, (iv) acts voluntarily, and (v) consents to the proposed action." The consent itself simply means that the client has the right to be told about a treatment or research in language that is easily understood and specifically told why it needs to be done, the risks or benefits, and alternative treatments. The client then has the right to refuse or allow the proposed treatment. The provider should not attempt to persuade or coerce the client to accept the treatment. The nurse is also obligated to

respect a client's opportunity to choose or decline a treatment. Not only does a client have the right to select the appropriate treatment, but the nurse must respect that choice once the decision is made (Walker, 2022).

Within the setting of medication administration, autonomy means clients have the right to refuse a drug that has been ordered for them. Although the nurse may perceive that the drug is good and will be beneficial to the client, the client may have a different viewpoint. That must be respected once the client is informed about the benefits and risks of a drug. This empowers the client to participate in their care, with the aim of better adherence to the overall plan of care.

Today, the shift is toward client-centered care. This empowers the client to be self-directed and still allows for a relationship with health care providers that encourages dialogue and partnership. This is particularly important for those with chronic diseases. Being part of a partnership and having a sense of empowerment increases safety, improves outcomes, and decreases costs (Lian et al., 2018). Other benefits are increased self-confidence on the part of the client and improved adherence to the medical regimen. An example of a model of client-centered care can be seen in Figure 3.2.

An essential component of choice or exercising autonomy is competence on the client's part. The client must have the *ability* to act autonomously. An individual who is not competent (someone who has been determined to be incompetent) may not be able to make a decision in their best interests because they cannot understand their own situation or the consequence of their decision. In this case, having a surrogate to make decisions would be in the client's best interests.

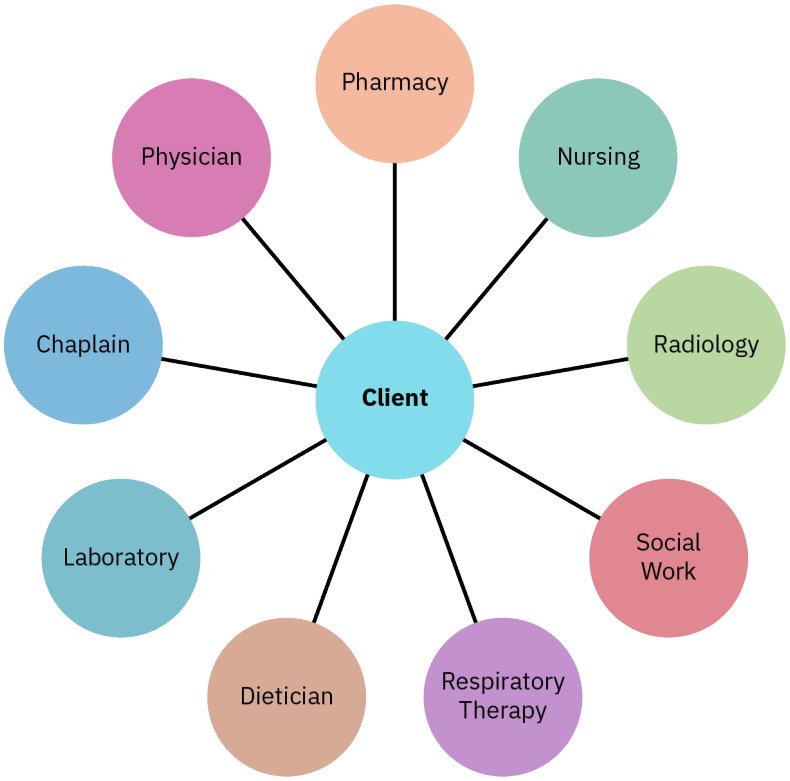


FIGURE 3.2 This is an example of a client-centered model of interprofessional care. All professions interact with each other and the client, but the client is at the center of the plan of care. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Beneficence

Beneficence is a principle that requires nurses to "do good" to actively promote their clients' health and well-being. They also must prevent and remove harmful situations that might affect their client. Beneficence implies an ethical obligation to abstain from injuring the client in any way, whether physically, psychologically, or morally. It involves mindfulness of the client's entire situation and needs.

Nonmaleficence

The principle of beneficence extends to **nonmaleficence**, which requires that nurses do no harm to the client and do

all they can to safeguard a client from harm. Obviously, intentional harm goes against the principles of beneficence and nonmaleficence; however, many acts performed by the nurse have the potential to cause harm unintentionally. For example, not all clients experience adverse effects of medications, but the potential is always there. A nurse could administer a medication hoping to make the client feel better, but an adverse effect may do the opposite and cause harm. An example of this might be a nurse who administers an opioid for a client's pain and then reevaluates the client 30 minutes later and observes that the client has developed respiratory depression.

When administering drugs to clients, the nurse must recognize that although the drugs are intended for good, all medications carry some risk to the client. Before any drug is ordered by the provider, the benefit of the drug versus the risk of the drug is considered. Before any drug is administered to a client, the benefit of the drug versus the risk of the drug is again weighed. The client should be fully informed of the benefits as well as the risks of any medication.

Justice

Justice is the principle relating to clients' fair and equitable treatment (Varkey, 2021). Each individual should be treated appropriately and equally. They should be allowed access to the same treatment and health care resources without prejudice or social discrimination. Even time can be a limited resource as it relates to visits with a provider because for more complex cases, more time might be necessary; however, that may shorten the time allotted to another client. The distribution of resources can be difficult to balance, especially when resources are limited (as in the case of organ transplantation) or in the case of uninsured clients. Justice is denied if an expensive medication would cure a client of their disease but a less expensive treatment was recommended because it benefits the provider in some way. Another example would be in the case of expensive drugs going only to those who have insurance or financial resources.

Veracity (Truth-Telling)

Veracity is important to building trust in the provider–client relationship (Varkey, 2021). The client should be able to ask the provider about their diagnosis, prognosis, and potential treatment. Refusing to divulge the truth to clients with a terminal diagnosis means that they are unable to finish important life tasks, say goodbye to loved ones, put financial affairs in order, or put their spiritual life in order (Fallowfield et al., 2002). When providers are not honest with clients, it may cause fear, confusion, or anxiety, especially in cases where the provider discloses the truth to the family but not the client.

ANA Code of Ethics

Obtaining a registered nurse (RN) license and entering the profession of nursing requires that nurse to meet the standards set out by the profession and made explicit by the American Nurses Association (ANA). Ethics are an integral component of the profession of nursing—the very bedrock of the profession. The purpose of the ANA Code of Ethics is to make clear the key goals, values, and responsibilities of the profession of nursing (ANA, 2015). The nine provisions of the ANA Code of Ethics are set forth in Table 3.2.

	ANA Code of Ethics Provisions	Drug Administration Example
Provision 1	The nurse practices with compassion and respect for the inherent dignity, worth, and unique attributes of every person.	The nurse educates the client about the drugs that are to be administered while considering the religious and cultural background of the client.
Provision 2	The nurse's primary commitment is to the patient, whether an individual, family, group, community, or population.	The nurse listens to the client and family about concerns regarding the prescribed medications.
Provision 3	The nurse promotes, advocates for, and protects the rights, health, and safety of the patient.	The nurse advocates for the client when the client's pain is not controlled by the medication ordered by the provider.

TABLE 3.2 **ANA Code of Ethics for Nurses** (source: https://www.nursingworld.org/practice-policy/nursing-excellence/ethics/code-of-ethics-for-nurses/)

	ANA Code of Ethics Provisions	Drug Administration Example
Provision 4	The nurse has authority, accountability, and responsibility for nursing practice; makes decisions; and takes action consistent with the obligation to promote health and provide optimal care.	The nurse withholds the medication and notifies the provider of assessments that suggest the medication ordered is not safe for the client at this time.
Provision 5	The nurse owes the same duties to self as to others, including the responsibility to promote health and safety, preserve wholeness of character and integrity, maintain competence, and continue personal and professional growth.	The nurse refrains from working overtime when fatigued.
Provision 6	The nurse, through individual and collective effort, establishes, maintains, and improves the ethical environment of the work setting and conditions of employment that are conducive to safe, quality health care.	The nurse educates the client about the medications prescribed but respects the decision of the client to take or refuse the drug.
Provision 7	The nurse, in all roles and settings, advances the profession through research and scholarly inquiry, professional standards development, and the generation of both nursing and health policy.	The nurse attends workshops and conferences in the area of specialty worked.
Provision 8	The nurse collaborates with other health professionals and the public to protect human rights, promote health diplomacy, and reduce health disparities.	The nurse collaborates with other disciplines, such as pharmacists and social workers, to obtain medications for home use.
Provision 9	The profession of nursing, collectively through its professional organizations, must articulate nursing values, maintain the integrity of the profession, and integrate principles of social justice into nursing and health policy.	The nurse knows and adheres to the policies and procedures of the institution. The nurse reports any errors made to the provider and management as soon as an error is known.

TABLE 3.2 **ANA Code of Ethics for Nurses** (source: https://www.nursingworld.org/practice-policy/nursing-excellence/ethics/code-of-ethics-for-nurses/)

When considering the aspects of drug administration and the ANA Code of Ethics, it is apparent that although the focus is on the goals and values of the nursing profession, the client is central to the process. This is tightly bound to the core ethical principles discussed in the previous section and is also tied closely to the client's safety, dignity, and well-being. The nurse should establish a caring relationship with the client built on trust and respect. This relationship should factor in elements such as culture, religious or spiritual beliefs, values, support systems, and sexual orientation or gender expression when planning the care of the client (ANA Code of Ethics, Provision 1.2, 2015). This provision goes on to say that the nurse should respect the client's decisions. Clients have the right to "accept, refuse, or terminate treatment without deceit, undue influence, duress, coercion, or prejudice, and to be given necessary support throughout the decision-making and treatment process" (ANA Code of Ethics, Provision 1.4, 2015). Nurses can educate the client and family without placing pressure on the client to accept the treatment or medication. Once the client has been given accurate and complete information about their condition and treatment options, they have the right to self-determination.

Benefit–Risk Ratio

Each provider prescribing, dispensing, or administering medications carefully assesses the benefits of a drug and its associated risks. Drugs are beneficial in many ways—they prevent, cure, and alleviate symptoms of disease—but drugs also carry risks associated with **adverse drug reactions** (ADRs). These reactions may be mild (e.g., headache, constipation, or nausea) or life-threatening (e.g., anaphylaxis, nephrotoxicity, or hepatic failure). The benefit–risk assessment is the analysis of the benefits and risks associated with a drug (Kürzinger et al., 2020). This assessment

is completed for each drug during research and continues throughout the lifetime of the drug. The health care provider also performs a benefit–risk assessment for each client prescribed a drug.

Risk can be defined as the probability of harm occurring as a result of an action—in this case, the administration of a drug. Benefit applies to the potential of a drug to treat the disease, ease suffering, or improve the quality of life. For example, the nurse administering a diuretic to a client with heart failure recognizes the benefit of the drug is to reduce the fluid that has accumulated in the lungs and improve the symptoms of shortness of breath; however, the risk may include loss of potassium or decrease in blood pressure (adverse effects). The risk is not the same for every client. In a client with an elevated potassium level and a normal or high blood pressure, the risk of the diuretic is minimal; however, if the client already has a low potassium level and low blood pressure, the risk will be higher. The provider makes a benefit–risk assessment based on the drug's probable benefits versus its potential risks. After drug therapy begins, the client is monitored to complete an ongoing evaluation of the benefit–risk balance. Ideally, the drug therapy continues as long as it is thought that the benefits outweigh the risks.

Drug Administration and Safety

Medication safety remains one of the most crucial challenges in institutions around the globe. There are many steps and many individuals involved in the process of a drug reaching the client. Most institutions have several processes in place to prevent a drug error from occurring, but not all processes are perfect, and no person is perfect. Many institutions have made the prevention of medication errors their number one priority, but errors continue to occur. The effects of a drug error are devastating and often long-lasting to the client, the client's family and friends, and the individual who made the error.

A *sentinel event* is defined by The Joint Commission (TJC) (n.d.-b) as "a patient safety event that results in death, permanent harm, or severe temporary harm." The harm may be physical or psychological in nature and is usually unexpected. These are events that should be reported immediately so that an investigation (called a root cause analysis) can be initiated without delay. Examples of the most common sentinel events are wrong-site surgeries, invasive procedures on the wrong clients, or death related to something other than the client's original illness. Administering medications to the wrong client that results in death or severe injury is another example of a sentinel event. An institution accredited by TJC must have policies in place to investigate and respond to sentinel events. The root cause analysis is helpful in identifying the underlying factors related to the harmful event and developing a plan to prevent another event. This process focuses primarily on system problems rather than individuals in an effort to improve the quality of care and safety of clients.

Adverse Drug Reactions

The World Health Organization (n.d., p. 1) defines an adverse drug reaction (ADR) as "harmful, unintended reactions to medicines that occur at doses normally used for treatment." Coleman and Pontefract (2016, p. 481) define an ADR as "unintended, harmful events attributed to the use of medicines." **Side effects**, a type of ADR, are considered to be secondary drug effects produced at therapeutic doses. An example of this might be sedation related to the use of an antihistamine or diarrhea related to the use of a stool softener. An **allergic reaction** is an immune response due to sensitivity to a specific drug. A mild allergic reaction can cause itching and rash, but **anaphylaxis** is a severe, life-threatening reaction causing dangerous bronchospasm and hypotension. These drug reactions affect the safety of the client but are not due to a medication error on the part of a health care provider.

TRENDING TODAY

Reporting Adverse Drug Reactions

It is important for the nurse to report adverse drug reactions. The U.S. Food and Drug administration (FDA) has a reporting mechanism in place through a portal called MedWatch for individuals (health care providers or consumers) to voluntarily report any adverse drug event. Each report is reviewed, and if a potential safety concern is identified, the FDA may take action—up to removing the drug from the market. Listen to this podcast from the FDA (https://openstax.org/r/newseventshuman) for more information about MedWatch.

Medication Errors

According to the National Coordinating Council for Medication Error Reporting and Prevention (2023), a **medication**

error is defined as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer." In 1999, a landmark report by the Institute of Medicine, *To Err Is Human*, increased awareness of medical errors in the United States. This report stated that as many as 98,000 people die in hospitals yearly due to medical errors. The following year this was validated with the clarification that medication errors in health care facilities are the most common type of these errors. This article describes 25 common medication errors in nursing and prevention recommendations (https://openstax.org/r/medicationerr).

The FDA receives more than 100,000 reports of drug errors each year, but more than 7 million clients in the United States are impacted by medication errors annually (da Silva & Krishnamurthy, 2016). Adverse drug events account for almost 700,000 emergency department visits each year (AHRQ, 2019b). The cost of caring for individuals whom a drug error has harmed exceeds $40 billion annually (Tariq et al, 2023). The financial and human costs of these errors are staggering.

An **adverse drug event** (ADE) is client harm resulting from exposure to a drug. This is injury from a medication, a missed medication, or an inappropriately dosed medication. It may or may not result from an error or poor-quality care. Medication errors that do not cause harm to a client (perhaps due to luck or the drug not reaching the client) are considered to be *potential* ADEs; in contrast, if harm to the client occurs, it is considered a *preventable* ADE. A drug can be prescribed, dispensed, and administered correctly, but the client may still experience an ADE. This is considered an adverse drug reaction (discussed in the previous section). This is an expected adverse outcome due to the drug's pharmacological action and is not always preventable (Tariq et al., 2023). Medication errors, however, *are* preventable.

If a physician orders an incorrect dose of a medication but the pharmacist catches the mistake before dispensing it, it is considered a medication error. If the physician orders the correct medication and dose but the pharmacist dispenses the wrong dose, it is a medication error. Errors may be related to any of the following (and this may not be an exhaustive list) (Tariq et al., 2023):

- Deteriorated drug
  - Product expired
  - Product stored incorrectly
- Error in prescribing
- Extra dose
- Insufficient monitoring
- Known allergen
- Known contraindication
- Omission of drug
- Wrong client
- Wrong dose
- Wrong diluent
- Wrong drug
- Wrong infusion rate
- Wrong preparation
- Wrong route
- Wrong strength or concentration
- Wrong time
- Wrong technique
  - Crushing an extended-release tablet
  - Administering a subcutaneous medication using an intramuscular technique

According to the Agency for Healthcare Research and Quality (MacDowell et al., 2021), medication administration is a very complex process characterized by the involvement of many health care team members, not just the nurse. Many institutions are working on ways to improve technology and workflow to make the process safer for the client. The manufacturer, packager, provider, pharmacist, technician, and nurse are all part of the process—and each is in a position to make an error. There are many different ways for an error to occur, but in the clinical setting, the nurse is

the final person in the chain able to prevent an error from occurring.

Some errors harm the client directly, but others may harm the client indirectly. Administering the wrong drug or doubling the dose of a medication may harm the client directly, whereas giving too little medication may cause a client to be undertreated and not take care of the disease, thereby causing harm indirectly. The most common types of lethal medication errors include giving an overdose of a medication, giving the wrong medication, and giving the drug by the incorrect route. Failure to monitor kidney or liver function can also impact the client's safety.

Causes of Medication Errors

Medication errors most commonly occur when the medication is being ordered or prescribed. It is estimated that as many as 50% of drug errors occur when the medication is ordered, and nurses and pharmacists identify 30%–70% of those errors (Tariq et al., 2023). Almost 75% of drug errors have been attributed to distraction (Tariq et al., 2023). The provider may be distracted by phone calls, speaking to family members, or other situations requiring their attention. The same may be true for the pharmacist who dispenses the drug or the nurse who administers it.

Some causes of medication errors can be related to human factors, communication errors, confusion over packaging, and confusion about medication names (Tariq et al., 2023). Human factors might include an incorrect drug calculation, a transcription error, a knowledge deficit, or a performance deficit, such as an incorrect drug administration technique. Communication errors may include illegible handwriting that causes an incorrect interpretation of an order, or misunderstood verbal or telephone orders. However, although human error may cause a medication error, the underlying issue may be the system itself. The system may be flawed and/or there may not be an adequate process in place to find mistakes (Tariq et al., 2023).

Prevention of Medication Errors

To prevent some of the previously described communication errors, many institutions have order read-back policies for verbal or telephone orders. The nurse or pharmacist first transcribes the order and then reads it back to the physician. Many institutions have policies recommending that if a written order is illegible, the pharmacist or nurse must call the provider to clarify rather than guess what the provider intended. Computerized order entry has decreased the incidence of illegible orders; however, there is still the chance that an incorrect dosage or route may be entered. Errors from the confusion of medication names occur because many drugs have names that sound alike or look alike, such as Celebrex, Cerebyx, and Celexa or dopamine and dobutamine. (See the List of Confused Drug Names (https://openstax.org/r/recommendations) from the Institute for Safe Medication Practices (ISMP) for more information.)

In the past, an individual was often blamed when medication errors occurred. Many errors were thought to be the result of procedural violations, negligence, or carelessness. As a result, individuals may have received disciplinary action (even firing), loss of license, or threat of a lawsuit. Institutions are slowly shifting their culture from "naming, blaming, and shaming" to "how can we improve the system to prevent errors." When shaming and blaming occur, it reduces the willingness of some individuals to come forward and acknowledge their mistakes. This may harm the client because the error is unreported, but it may also lead to another person making the same error if the fault is in the system. There has been a gradual move to a "just culture," which refers to a system of shared accountability. The organization may not have provided adequate training or had inadequate policies and procedures in place, or poorly designed units. In a just culture, the organization is accountable for the system or process it has designed as well as behaviors. Ideally, organizations will move away from policies that require punishment for errors and focus on reinforcing principles that decrease "at-risk" or reckless behaviors.

James Reason (2000) developed the Swiss cheese model (see Figure 3.3), which drew attention to the occurrence of client harm as a result of failures in the health care system itself. Each barrier to client harm has a weakness (or hole); thus, Reason likened this to Swiss cheese. When all of the holes are aligned, the hazard (in this case, a medication error) reaches the client, and harm will occur. Figure 3.3 depicts an example of the Swiss cheese model using a prescribed medication moving through the layers of holes until the client is harmed. This model could be applied to any harm related to client care, not just errors in medication administration. This model focuses on the health care system rather than the individual in the occurrence of medical errors. Improving the safety of the client must begin with developing a culture of safety within the institution. The emphasis should be on working together as a team, collaborating with a focus on communication and client safety.

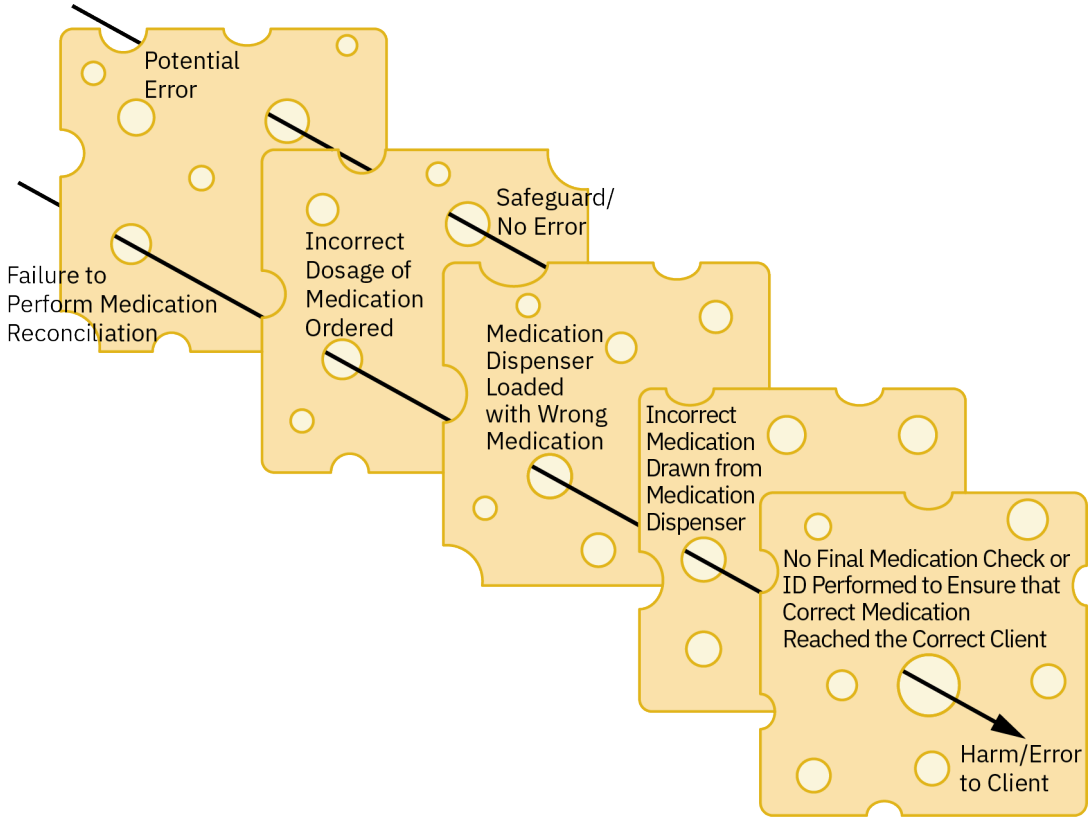


FIGURE 3.3 This version of Reason's Swiss cheese model depicts how an incorrect medication may be given to a client. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Many institutions have begun the process of developing strategies to prevent or reduce the number of medication errors (https://openstax.org/r/psnet.ahrqgov). Some strategies include (Tariq et al., 2023):

- Replacing handwritten orders with computerized order entry
- Rounding with the physician (pharmacist/nurse)
- Double-checking the dose of all high-alert medications with another provider
- Double-checking drug calculations
- Speaking with the pharmacist or looking the drug up in a resource if unsure about a medication
- Remembering that *any* drug has the potential for adverse effects
- Monitoring kidney and liver function
- Knowing high-risk medications
- Knowing the indication of a prescribed drug (if not known, then asking the provider)
- Order read-back and verification of verbal or telephone orders
- No use of abbreviations
- Providing clear, explicit instructions for each medication

Other potential strategies include:

- Bar code systems
- Instituting medication reconciliation at any transition in care

Some medications have an increased likelihood of causing harm to the client if administered incorrectly, such as potent blood thinners like heparin or insulin, which may cause a bleeding event or lethal drop in blood sugar, respectively. The ISMP has classified these drugs as "high-alert" medications (https://openstax.org/r/ismporg). These are drugs that should have two providers verify the dose to be administered, and both nurses must document on the medication administration record (MAR) when these medications are given.

The ISMP has several strategies for the prevention of medication errors. Improving access to information about drugs is helpful to any provider. This may take the form of drug books or guides on the unit or access to relevant

electronic resources. Another prevention strategy is limiting access to high-alert medications. Some high-alert medications, including neuromuscular blockers, are not needed on each hospital unit, so removing access to them on those units may help avoid dangerous drug errors. The more standardized the systems for ordering, storing, preparing, or administering medications, the less likely an error will occur. The electronic system has automated alerts to prevent errors (e.g., pop-up alerts to prevent administering a medication that a client is allergic to). "The responsibility for accurate medication administration does not lie with a single individual. Rather, it lies with multiple individuals, including organizational leaders, who are responsible for the design, implementation, and maintenance of reliable systems to support safe medication use for all practitioners" (ISMP, 2023).

3.3 Documentation and Informatics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 3.3.1 Discuss the Quality and Safety Education for Nurses (QSEN) competencies.
- 3.3.2 Explain the Joint Commission "Do Not Use" abbreviation list as it relates to drug administration.
- 3.3.3 Describe how information technology affects drug administration and error prevention.

Quality and Safety Education for Nurses (QSEN) Competencies

As mentioned earlier, in 1999 the Institute of Medicine published its report, *To Err Is Human*, regarding the number of errors impacting clients within the health care system. Health care systems are incredibly complex, and that very complexity lends itself to error. In response to these concerns, the American Association of Colleges of Nursing (AACN) and the Robert Wood Johnson Foundation developed the Quality and Safety Education for Nurses (QSEN) initiative. The primary focus of QSEN (https://openstax.org/r/qsenorgco) is to develop a culture of safety by maximizing system effectiveness and individual performance (Barnsteiner & AACN, n.d.). To address this, QSEN, in alignment with AACN, created several learning modules or competencies focusing on quality and patient (or client) safety. AACN/QSEN now incorporates the AACN Essentials. The modules aim to educate nurses and nursing students to minimize the risk of harm to clients and providers. This is done by showing learners how to examine system effectiveness and individual performance (Barnsteiner & AACN, n.d.). These competencies include (AACN, n.d.):

- Patient-centered (client-centered) care
- Teamwork and collaboration
- Evidence-based practice (EBP)
- Quality improvement (QI)
- Safety
- Informatics

Some common errors in health care include incorrect medication administration, wrong site surgeries, diagnostic inaccuracies, equipment failures, and system failures, to name a few (Barnsteiner & AACN, n.d.). Errors that are a result of system failures and system design are called *latent errors*; in contrast, *active errors* are errors that are made by individual clinicians (Rodziewicz et al., 2023). These errors may occur from unintentional or intentional risk-taking behaviors. Unintentional "at-risk" behaviors are usually not perceived as risky, and the individual usually believes that they are making a safe choice. This could be a situation in which the nurse has two clients whose conditions suddenly deteriorated at the same time that an admission came on to the unit and an error occurred, or an experienced nurse who programs an IV pump outside of the pump drug library to save time (Barnsteiner & AACN, n.d.; ISMP, 2020). An intentional risk-taking behavior could be a nurse who purposely chose not to identify a client prior to giving medication. They are knowledgeable about the institutional process but choose not to practice it. When attempting to prevent errors, it is important to address the cause of the errors rather than use blanket strategies that may or may not be effective.

The AACN states that it is important to have a culture of safety to counter the fact that all caregivers are human. Some of the elements of a culture that promotes safety are shared values and goals, collaboration, and openness and transparency regarding errors. Client involvement is crucial in this process so that they question a provider when they do not wash their hands, observe any unsafe behavior, or question a medication.

The Agency for Healthcare Research and Quality (AHRQ, 2019a) asks for organizations to commit resources to

address safety concerns. The AHRQ encourages institutions to set up blame-free environments for individuals so they are able to report errors or near-misses without fear of punishment. A blame-free environment allows the client to obtain quality care quickly in order to minimize harm. (For more information, see the AHRQ website (https://openstax.org/r/programsind).)

SPECIAL CONSIDERATIONS

Safety

QSEN strategies for promoting a culture of safety include:

- User-centered design, such as wearing a vest that identifies the nurse when administering medications, so as to prevent interruptions
- Attending to work safety—it is important to realize there are limits to the number of hours an individual can work and be safe
- Avoiding relying entirely on vigilance
- Use of checklists
- Training health care professionals to function together as a team
- Improving access to accurate, timely information
- Involving clients in their care
- Anticipating the unexpected
- Designing and having a plan for recovery from an error

(Source: Barnsteiner & AACN, n.d.)

The nurse should encourage clients to become active participants in their care. Each and every health care professional needs to make safety one of their primary responsibilities (Barnsteiner & AACN, n.d.).

Documentation

The client record is one of the primary means of communication between health care providers. Having current, effective communication within the health record (either the EHR or the paper record) is key to the client's safety and quality of care. Communication between disciplines may occur verbally through physician rounds or handoffs during shift report. It also may occur through provider orders or notes within a paper chart or EHR. When members of the health care team make an entry into the record, it is known as charting or documentation. Documentation should be accurate and timely, occurring near the time the provider made an observation or completed an intervention, such as medication administration. That said, it is important to document at the time or slightly after rather than before.

It is crucial that all providers remember that the chart is a legal document that provides proof of the client's status and the care that was delivered. Although components of documentation are similar between facilities, most institutions have their own policies about who can document within the record, how it is done, and when it should be completed. The nurse should adhere to these standards and remember that these records should be kept confidential.

One area in which the health care team should be alert to potential errors is any transition of care for the client. A transition of care includes the client's admission to the hospital, transfer to another unit, and discharge home. Transitions of care are critical times that increase a client's risk for medication errors. Often numerous changes in medications occur when a client is admitted to the hospital setting. Medication reconciliation should be completed at any transition of care or outpatient visit, especially when more than one provider is orchestrating the care of the client. Medication reconciliation should occur whether a paper or an electronic record is used.

Reconciling medications is one of the Joint Commission's National Patient Safety Goals for documentation and is considered evidence-based practice in improving client safety (Joint Commission, 2023). The nurse compares the list of medications the client is taking or is supposed to be taking with the list of newly ordered medications. Once this is completed, the nurse identifies discrepancies between the two lists, clarifies any differences, and attempts to resolve any problems between the two by communicating with the client or family, the provider, and the pharmacist. Potential problems that may be identified include (1) the omission of a drug, (2) discrepancies between frequency or

dosing, (3) duplicate drugs (this may happen when one provider orders a generic form of the drug and another provider orders by brand name), (4) contraindications, or (5) incorrect drugs. The nurse should instruct each client to carry a list of current medications with the dosage and frequency at all times. Ensuring that the client understands the changes to their medications is key to adherence to the medical regimen and the client's health. The use of technology such as the EHR can provide solutions to the challenges of managing medications during transition points (Vaghasiya et al., 2023).

Although 98% of all facilities have some form of EHR, some facilities still rely on the paper record (Apathy et al., 2021). To complete medication reconciliation in a paper record, the medication administration record (MAR) is compared to the physician's orders for accuracy once each shift. The nurse then signs off that there are no discrepancies between the ordered or discontinued medications and the MAR. As mentioned previously, if any discrepancies are found, the nurse takes the appropriate steps to resolve them.

Another key element in charting is client teaching. Each discipline should document any teaching that is performed, including when it occurred and who did the teaching. It should also include the topics discussed and the response to the education. Was the client receptive? Did the nurse evaluate the client's learning, and how was this done? Could the client demonstrate knowledge or "teach back" the information to the nurse? Once teaching is documented, it is also important to make recommendations about how others can reinforce the already accomplished teaching.

The Joint Commission "Do Not Use" Abbreviations

The Joint Commission (TJC) was founded in 1951, and its aim is to improve health care for the public through evaluating and accrediting health care institutions across the United States. It surveys institutions every three years to ensure they meet standards of compliance. All surveys are unannounced and are conducted by experts in the health care field, such as physicians, nurses, and hospital administrators. The primary foci of TJC are safety and quality of care. TJC has more than 250 standards that it expects institutions and health care workers to address. Some of these standards focus on medication management and the prevention of medication errors. In an effort to eliminate the use of potentially dangerous abbreviations and acronyms, TJC published an official "Do Not Use" list of abbreviations as part of its 2004 National Patient Safety Goals.

The following is a list of abbreviations that should never be used (Joint Commission, n.d.-a):

- *U, u:* Use "unit."
- *IU:* Use "International Unit."
- *Q.D., QD, q.d., qd:* Use "daily."
- *Q.O.D., QOD, q.o.d., qod*: Use "every other day."
- *MS:* Use "morphine sulfate."
- *MSO_4:* Use "morphine sulfate."
- *$MgSO_4$:* Use "magnesium sulfate."
- *Always* use leading zeros! Naked decimals (.4 mg or .1 mg) may result in medication errors because they can be interpreted as 4 or 1. Instead, write 0.4 mg or 0.1 mg.
- *Trailing zeros (e.g., 3.0 g, 50.0 mg):* Missed decimals result in medication errors. Instead, write 3 g or 50 mg.

There are important exceptions to the use of trailing zeros: It is acceptable to use a trailing zero in the case of reporting laboratory values, when measuring lesions, when denoting the size of catheters and tubes, or in imaging studies. However, trailing zeros should never be used when writing medication orders or documenting dosages (Joint Commission, n.d.-a).

The Institute for Safe Medication Practices (ISMP) is a nonprofit organization whose goal is to educate health care providers and consumers about safe medication practices. The nurse should refer to the ISMP for a more complete list of error-prone abbreviations (https://openstax.org/r/sitesdefaultfil), symbols, and dose designations.

Nursing Informatics

Understanding the tools and developing the knowledge necessary to function are crucial to success in the current digital age. A growing specialty within nursing that integrates health information technology (HIT) and supports this understanding is nursing informatics. The American Nurses Association (ANA, 2022, p. 3) defines nursing

informatics (NI) as "the specialty that transforms data into needed information and leverages technologies to improve health and health care equity, safety, quality, and outcomes."

Modern technology is now an essential component of health care. A health information system integrates data collection, processing, and reporting through information technology in order to improve system effectiveness and efficiency (Torab-Miandoab et al., 2023). Essentially, it transforms information from a paper-based system into an electronic health record (Tian et al., 2019). Health information technology (HIT) ideally allows for better coordination of care and improved organization of information, timeliness, and accuracy (Torab-Miandoab et al., 2023). Torab-Miandoab and colleagues (2023) go on to say that other advantages of HIT are decreased medical errors, decreased cost, ease of information exchange, and ease of access for providers.

The amount of information the nurse and other health care professionals collect and process at the bedside is extensive. Once a client is assessed and the information is collected, it goes into the EHR database. That information will evolve throughout the hospital stay and beyond. The unique aspect of informatics as it relates to nursing, and health care in general, is the need to use the principles of computer and information science combined with those of nursing science. Communication is also a part of this process—communication between disciplines, institutions, clients, and insurance companies as well as between devices. For example, many devices within an institution communicate with the EHR, including lab applications, glucose monitors, pulse oximeters, and even devices that track clients throughout the hospital.

Electronic Health Record

Most institutions rely on the electronic health record (EHR) as each client's primary health information source. Technology now allows this record to serve as the vehicle for communication between each health care team member and even across institutions. According to Campanella et al. (2016, p. 1), "an EHR may also include a decision support system (DSS) that provides up-to-date medical knowledge, reminders or other actions that aid health professionals in decision making." The client's demographics, status, assessments, the type of care provided, and progress throughout the stay are provided through the EHR. The nurse provides documentation for the assessments completed, nursing interventions, teaching, and observations made throughout their shift. The electronic medication administration record (eMAR) is a part of the EHR and serves as the official documentation for the medication administered or withheld by the nurse. The EHR is a legal document and must be kept current as events occur during the stay. Documentation of medications administered or withheld should also be done in real time to protect client safety. After discharge, the record is kept within the institution and can be accessed during subsequent admissions or for insurance purposes, according to institutional policy. Each institution has its own unique EHR, though they have similarities.

SPECIAL CONSIDERATIONS

Typical Elements of the EHR

- Client summary
- Order section (with e-prescribing, or CPOE)
- Allergy section
- History and physical section (e.g., medical histories), including consults
- Physician progress notes
- Nurses' notes
- Laboratory reports
- Radiology reports
- Diagnostic tests
- Graphic report (vital signs, intake and output, daily weights)
- Medication profile and eMAR, drug–drug interactions, food–drug interactions
- Client education record/printable educational materials
- Administrative and billing data

(Sources: Campanella et al., 2016; HealthIT.gov, 2019)

Most hospitals and health care institutions across the country have adopted the use of EHRs, and many providers

now have a working knowledge of the technology needed to operate those systems. Some important features usually contained in the EHR are described in the following sections.

Computerized Prescriber Order Entry (CPOE)

An important aspect of the EHR is e-prescribing, also known as **computerized prescriber order entry (CPOE)**. This allows the provider to prescribe medications through electronic means to a nurse and pharmacist on the unit or to a pharmacy miles away from the provider. The advantages of CPOE are the ability to verify other medications the client is taking, screening for possible drug–drug interactions, and hard stops in the system that prevent the medication from being ordered when contraindicated. E-prescribing also allows the provider to improve the safety of pain management when ordering a controlled substance because it reduces the opportunity for forgery, and it is easier to identify when multiple providers order the same controlled drug (Mandeville et al., 2020). Despite the CPOE often reducing some types of errors, it may enable other forms of errors. For example, CPOE has been linked to many HIT errors that have caused adverse events (Amato et al., 2017), including: (1) wrong drug ordered, (2) time delays with the client receiving the medication, (3) duplicate drug ordered, (4) prescription sent to the wrong pharmacy, (5) wrong dose, and (6) unidentified allergy.

System alerts are often built into the EHR to assist with error prevention and help with clinical decision-making. Alerts in the EHR may improve treatment effectiveness, assist with decision support, and act as effective reminders for best care. For example, when a client is admitted with a stroke, the EHR may prompt the physician to order a computerized axial tomography (CAT) scan of the brain to assist with the diagnosis. The alert may appear as a small dialog box that allows the user to click OK or Cancel. One frequently seen alert regarding medication administration pops up to inform the nurse of a client's drug allergies. Other alerts will notify the nurse administering medications of a potential mix-up with look-alike and sound-alike drugs. The system will identify high-alert medications requiring a second nurse to double-check the first nurse. A nurse administering medications may find that the pharmacy has provided a 25 mg form of a tablet, but the order is for 50 mg. An alert will notify the nurse to give two tablets instead of one, thus preventing a medication error. The system may also flag the nurse with instructions on how to dilute or reconstitute medications.

There are two types of alerts. A *hard-stop alert* is one in which the user is not allowed to proceed without taking some kind of action. The aim of a hard-stop alert is to improve quality of care and quality outcomes; unfortunately, they may cause a delay in care, especially if used frequently in the EHR. A *soft-stop alert* is one in which the alert is acknowledged, but the user may proceed. Both soft- and hard-stop alerts can be useful to the provider, but when "workarounds" are performed, it can place the client at risk. A workaround is a way of handling a problem or making something work without fixing the problem. One example of a workaround is a nurse having difficulty getting the barcode scanner to work, so the nurse types the client's name and medical record number into the system to manually document the medication administration. Although the client is able to get the drug, the problem is not solved. It may bypass safety measures in the system, placing the client at risk. Another unfortunate consequence of multiple alerts is alert fatigue because it interrupts workflow (Powers et al., 2018).

Barcode Scanning

Many institutions have implemented barcode-assisted medication administration as a means to reduce errors at the bedside. This technology is used to verify and document medication administration at the bedside. Once the nurse scans the barcode on the client's wrist, it identifies the client and opens the eMAR, which informs the nurse as to which medications should be administered. The nurse then scans the barcode on the medication, which should match the medication and the appropriate dose to be administered. If it corresponds to the client's record, the medication can then be administered. If it is incorrect, the nurse will receive an electronic alert.

Recording Adverse Drug Events Through the EHR

As mentioned previously, adverse drug events (ADEs) are a substantial problem in health care. Clients have complicated health histories, and care is very complex. Most hospitals rely on the voluntary reporting of ADEs, though few are actually reported (Murphy et al., 2023). The EHR can help obtain information on ADEs in hospitalized clients. An advantage to this is an improved ability to predict the occurrence of an ADE in future clients. The ability to identify ADEs earlier can increase client safety.

Patient (Client) Care Portals

Informatics has changed the way health care providers take care of the client, and it has changed the way that

clients interact with health care providers. Many providers have patient (client) care portals that allow communication between provider and client, eliminating the need for face-to-face visits. Many applications (apps) available on phones or smartwatches can assist the client and provider in monitoring the client's health, such as pulse rate and rhythm monitoring, blood pressure, and blood glucose monitoring, to name a few.

Chapter Summary

This chapter discussed federal legislation affecting health care and the electronic health record. The state nurse practice acts and the formation of boards of nursing also were explained. The ethical principles of autonomy, beneficence, and nonmaleficence were examined, as was their role in nursing practice. A thorough discussion of medication safety and strategies to prevent medication errors was provided. The chapter concluded with a review of nursing informatics and its role in health care.

Key Terms

adverse drug event (ADE) any harm to a client that occurs from exposure to a drug

adverse drug reaction (ADR) a noxious, unintended, and undesired effect that occurs at normal doses of the drug

Affordable Care Act (ACA) a law enacted in 2010 to make health insurance available to more Americans

allergic reaction an immune response due to sensitivity to a substance that may cause itching and rash

anaphylaxis a severe, life-threatening reaction causing serious bronchospasm and hypotension

autonomy being independent and having the freedom to choose

beneficence an ethical principle requiring an individual to "do good" to others

computerized prescriber order entry (CPOE) the prescription or ordering of drugs through the electronic health record (EHR)

confidentiality the assurance that the client will not have their personal health information (PHI) disclosed without their consent

Health Information Technology for Economic and Clinical Health (HITECH) Act a law enacted to improve the efficiency and quality of care through the adoption of electronic health records

Health Insurance Portability and Accountability Act (HIPAA) a law that protects the privacy and confidentiality of an individual and prevents insurance companies from refusing to cover those with preexisting conditions

justice an ethical principle relating to clients' fair and equitable treatment

medication error any preventable event that may cause or lead to inappropriate medication use or client harm while the medication is in the control of the health care professional, client, or consumer

nonmaleficence an ethical principle that holds that individuals have an obligation to do no harm to others

protected health information (PHI) any information by which an individual can be identified (name, date of birth, Social Security number, phone number, address, etc.) as it relates to their health condition, provision of care, or payment

side effects secondary drug effects at the therapeutic drug level (e.g., sedation that occurs with a benzodiazepine or opioid)

veracity an ethical principle requiring an individual to tell the truth

Review Questions

1. What information is important for the nurse to recognize about the Health Insurance Portability and Accountability Act (HIPAA)?
   a. Client outcomes can be improved through the use of quality measures.
   b. Nurses are mandated to use the electronic health record in a meaningful way.
   c. Personal health information (PHI) should not be disclosed except on a need-to-know basis.
   d. This act expanded the Medicaid program by raising the federal poverty level.

2. What ethical principle refers to promoting potential benefits and decreasing potential harms when the nurse provides care to a client?
   a. Justice
   b. Nonmaleficence
   c. Autonomy
   d. Beneficence

3. What ethical principle is the nurse practicing when the nurse respects a client's wish to choose a specific treatment?
   a. Justice

b. Nonmaleficence
c. Autonomy
d. Beneficence

4. What is a potential benefit to respecting a client's autonomy in their health care decisions?
a. Improves outcomes
b. Decreases the likelihood of the client refusing treatment
c. Removes harmful conditions
d. Decreases the chance of the client denying their illness

5. A nurse is completing their eighth 12-hour shift in a row. Which item from the ANA Code of Ethics is the nurse at risk of violating?
a. The nurse should practice with compassion and respect for the inherent dignity, worth, and unique attributes of the clients.
b. The nurse owes the same duty to self as to others, including the responsibility to promote health and safety.
c. The nurse's primary commitment is to the client, whether an individual, family, group, community, or population.
d. The nurse collaborates with other health care professionals to protect human rights, promote health diplomacy, and reduce health disparities.

6. The nurse is caring for a client receiving medication for the treatment of high blood pressure. What term *best* describes the client's report to the nurse of becoming dizzy and passing out after taking this medication?
a. Anaphylaxis
b. Allergic reaction
c. Adverse drug reaction
d. Adverse drug event

7. The nurse, caring for a client with a seizure disorder, was late in administering the antiseizure medication, resulting in the client having a seizure. What term best describes this event?
a. Adverse drug reaction
b. Allergic reaction
c. Side effect
d. Adverse drug event

8. The nurse contacts a provider for a medication order, and the provider enters the order electronically from a remote computer. This is best described as what type of technology?
a. Health information technology (HIT)
b. Protected health information (PHI)
c. Computerized prescriber order entry (CPOE)
d. Electronic health record (EHR)

9. The nurse recognizes that alerts have been placed into the electronic health record for what purpose?
a. To improve the safety of the client
b. To assist with communication with other providers
c. To allow orders to be communicated to other departments
d. To decrease the need for barcode scanning

10. The nurse is reviewing orders just written by the health care provider. Which order would the nurse identify as being written correctly?
a. Carvedilol .625 mg
b. Carvedilol 0.625 mg daily
c. Carvedilol 25.0 mg daily

d. Carvedilol 1.250 mg daily

CHAPTER 4
Introduction to Homeostasis

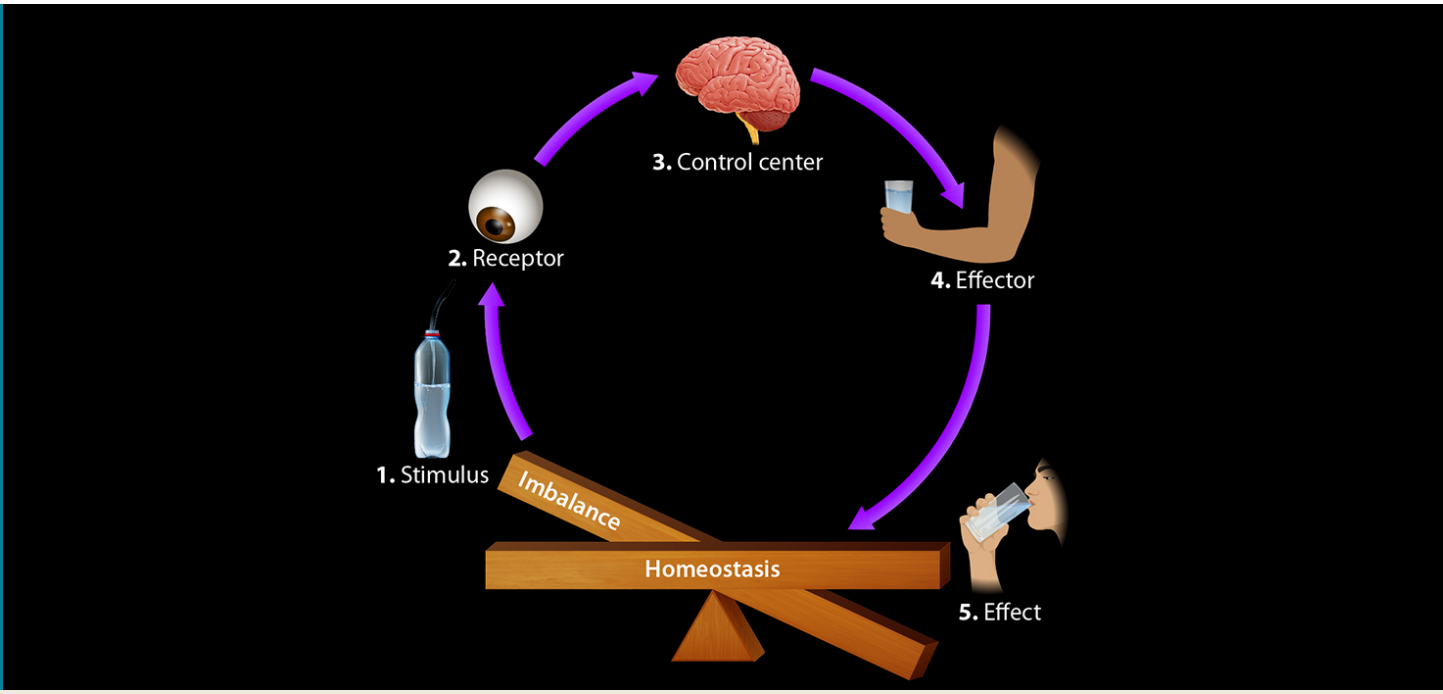


FIGURE 4.1 The nervous system sends chemical and electrical messages between the brain and other parts of the body to control homeostasis (a state of stable equilibrium between physiological processes), physical reflexes, and both voluntary and involuntary activities. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Homeostasis is important in helping the body maintain a stable environment. It involves the regulation of physiologic processes. This process is achieved through the coordination of different organ systems and feedback mechanisms. This chapter will provide an overview of homeostasis and these feedback mechanisms.

4.1 What Is Homeostasis?

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 4.1.1 Define homeostasis.
- 4.1.2 Compare and contrast intracellular fluid and extracellular fluid and their effects on the body's cells.
- 4.1.3 Discuss the major cations and anions and their essential functions.

Homeostasis is the ability of the body to maintain a stable and constant internal environment despite changes in the external environment (Billman, 2020). This means that the body can regulate and balance its various physiologic processes, such as body temperature (see Figure 4.2), fluid balance, pH levels, blood sugar levels, and hormone levels, to ensure they remain within a narrow range that is optimal for the body's functioning.

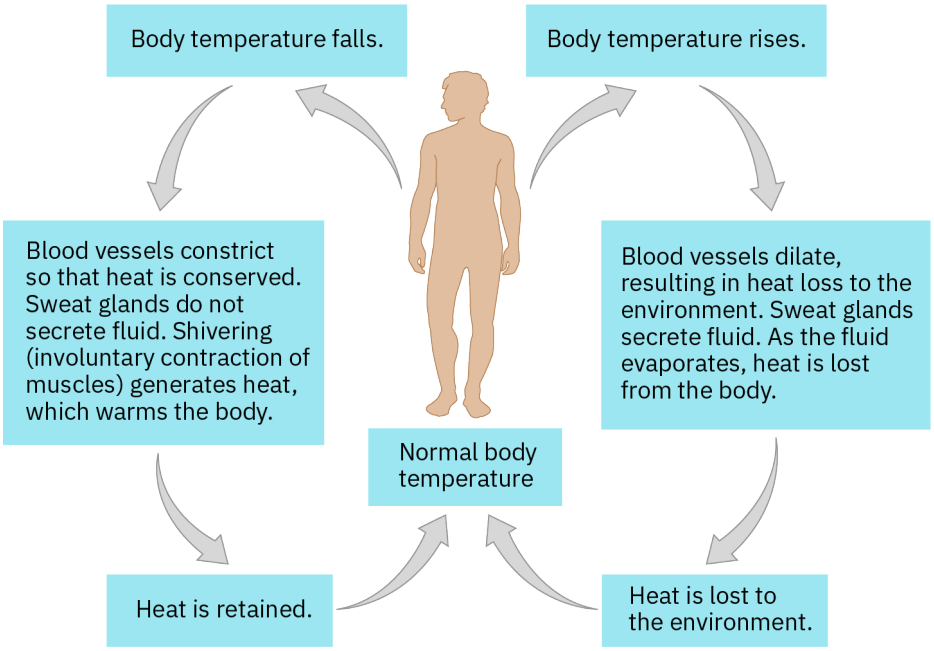


FIGURE 4.2 The human body is maintained by complex mechanisms that keep it in balance to promote physiologic function. (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Homeostasis

Homeostasis is a fundamental process that enables the body to maintain a stable internal environment in the face of constantly changing internal and external conditions. Disruption of homeostatic mechanisms may cause diseases and severe impacts on physiologic well-being. Two key principles govern homeostasis: fluid balance and electrolyte balance.

The first principle of fluid balance involves maintaining the body's fluid compartments in **osmotic equilibrium**, except for **transient change**. This means that the concentration of **solutes** in each compartment is carefully regulated to prevent water from flowing into or out of cells, which could disrupt cellular function (Koeppen & Stanton, 2023; Valls & Esposito, 2022).

The second principle of electrolyte balance involves ensuring that the numbers of **ions** (**anions** or **cations**) within each compartment of the body are balanced and electrically neutral. Each compartment works to maintain a constant volume of fluid and to replace and exchange ions to maintain this neutrality (Koeppen & Stanton, 2023; Valls & Esposito, 2022). This helps ensure that the body's pH remains within a narrow range, which is essential for proper physiologic functioning.

SPECIAL CONSIDERATIONS

Homeostasis in Children, Pregnant Clients, and Older Adults

Children have unique physiologic characteristics and developmental needs. Children have a relatively higher water requirement compared with adults because of their higher metabolic rate and larger proportion of body water. Children are also more likely than older individuals to become dehydrated because their kidneys are less efficient at conserving water. Electrolyte balance in children may be more susceptible to imbalances because of their immature kidneys, resulting in higher renal losses of sodium and potassium.

Pregnancy brings about significant physiologic changes that impact homeostatic mechanisms. Pregnancy increases blood volume and fluid retention to support the developing fetus. Hormonal changes influence fluid balance, causing the client to be more susceptible to edema and electrolyte imbalances. Increased levels of progesterone can also affect electrolyte regulation. Changes in kidney function and the demands of the developing fetus may impact the delicate balance of sodium, potassium, and calcium.

As individuals age, various physiologic changes occur. Older adults often have a reduced sense of thirst and may not drink enough fluids, leading to an increased risk for dehydration. Age-related changes in the kidneys can also affect water and electrolyte regulation, resulting in a higher risk for imbalances such as hyponatremia (low sodium) and hyperkalemia (elevated potassium).

Homeostasis is a complex mechanism that requires an integrated control system for self-regulation. It is primarily governed by a **feedback loop** that involves three key components: the receptor, the control center, and the effector (Figure 4.3).

- The **receptor** is a sensory organ that detects changes in the internal or external environment of the body. It sends signals to the control center when it detects a change that needs to be corrected.
- The control center is typically located in the brain or other part of the nervous system. It receives the signals from the receptor and processes them to determine the appropriate response. The control center then signals the effector.
- The **effector** is the part of the body that carries out the response. It could be a muscle, gland, or organ that alters its activity to counteract the initial change detected by the receptor.

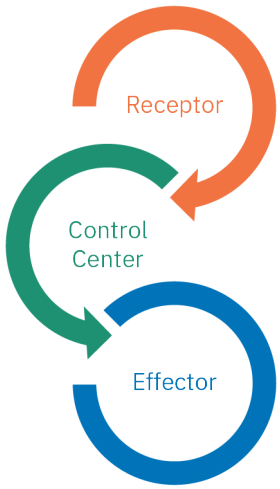


FIGURE 4.3 Feedback loops involve a receptor to a stimulus, the control center, and the effector that carries out the control center's response. (credit: reproduced with permission of Tina D. Barbour-Taylor)

The feedback loop plays a critical role in maintaining a balanced internal environment in the face of changing internal and external conditions (Hannezo & Heisenberg, 2019; Molnar & Gair, n.d.). By detecting and correcting deviations from the set point, the body is able to ensure that its various physiologic processes are functioning optimally, thereby promoting overall health and well-being.

Cellular Compartments

Sixty percent of the total body weight is composed of water. The body separates this water into two main fluid compartments: one that contains **intracellular fluid** and one that contains **extracellular fluid**. The fluid compartments work together to maintain fluid and electrolyte balance within the body. The movement of water and electrolytes between the compartments is regulated by various mechanisms, such as **osmosis** and **active transport** (Libretti & Puckett, 2023; Molnar & Gair, n.d).

The body strives to maintain a balance between the fluids in the compartment to ensure that the cells are surrounded by an environment that allows them to function optimally, as can be observed in Figure 4.4. The concentration of ions, such as sodium, potassium, and chloride, is carefully regulated in each compartment to maintain the proper **osmotic pressure**, which is the pressure needed to prevent water from flowing into or out of cells.

Disruptions in the fluid compartments, such as excessive fluid loss or retention, can lead to various health problems, including dehydration or edema. By regulating the equilibrium of body fluids, the body can guarantee the optimal operation of its diverse physiologic functions, thereby enhancing overall health and well-being.

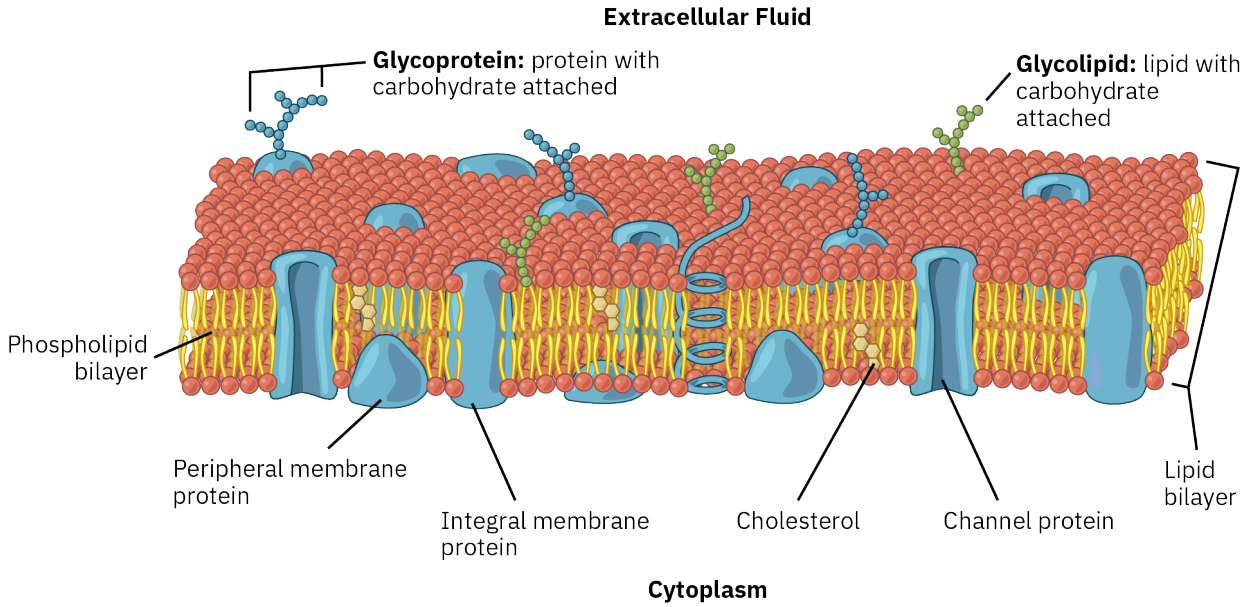


FIGURE 4.4 The cell membrane is a semipermeable membrane that allows for the homeostasis of intracellular and extracellular fluid compartments. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Intracellular Fluid

Intracellular fluid, also known as **cytoplasm**, refers to the fluid contained within the cells of the body. As shown in Table 4.1, intracellular fluid accounts for approximately 40% of the total body fluid in adults, and it plays a critical role in many physiologic processes.

The composition of intracellular fluid is tightly regulated to ensure that it provides an optimal environment for cellular function. It contains various electrolytes, such as potassium, magnesium, and phosphate ions, as well as proteins and other molecules essential for cell function.

Extracellular Fluid

Extracellular fluid is the fluid that surrounds the cells of the body, including fluid in the blood vessels and the fluid in the spaces between tissues and organs. It accounts for approximately 20% of the total body fluid in adults.

Extracellular fluid contains various electrolytes, such as sodium, chloride, and bicarbonate, as well as proteins, hormones, and other molecules.

The extracellular fluid is divided into three subcompartments. The **interstitial compartment**, which surrounds the tissue cells, makes up approximately 15% of fluid volume; the **intravascular compartment**, which contains the plasma and blood, makes up approximately 5% of fluid volume; and the **transcellular compartment** makes up approximately 1% of fluid but is generally not included in fluid volume calculations.

Transcellular Compartment (Third Space)

The transcellular compartment, also known as the third space, refers to a small volume of fluid that is contained within certain body cavities and structures, such as the pleural cavity, peritoneal cavity, and joint spaces. This compartment is separate from the intracellular and extracellular fluid compartments and is characterized by its limited communication with the rest of the body. The volume of fluid in the transcellular compartment is regulated by various mechanisms, including pressure and transport mechanisms, which ensure that it is in balance with the other fluid compartments. Table 4.1 lists fluid compartments and their volumes and major electrolytes for an adult.

Fluid Compartment	Fluid Volume	Electrolytes	
		Major Anions	**Major Cations**
Intracellular fluid	~40%	Phosphate	Magnesium Potassium Sodium
Extracellular fluid Interstitial fluid Intravascular fluid Transcellular fluid	~20% total (of the below areas) 15% 5% 1%	Chloride Phosphate	Calcium Magnesium Potassium Sodium

TABLE 4.1 **Adult Body Fluid Volumes and Electrolytes**

Ions

An ion is an atom or molecule that has an unequal number of protons and electrons. This inequality gives the ion an electrical charge, either positive or negative. Ions are critical to maintaining homeostasis within the body.

Anions

An anion is a negatively charged ion, meaning it has more electrons than protons. This happens when an atom gains one or more electrons, leaving it with a negative net charge. Chloride (Cl^-), bicarbonate (HCO_3^-), phosphate (PO_4^-), and sulfate (SO_4^-) are anions.

Cations

A cation is a positively charged ion, meaning it has fewer electrons than protons. This happens when an atom loses one or more electrons, leaving it with a positive net charge. Calcium (Ca^{2+}), magnesium (Mg^{2+}), potassium (K^+), and sodium (Na^+) are cations. Cations are important for acid–base reactions (reactions that affect pH).

4.2 Osmolality

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 4.2.1 Describe osmolality.
- 4.2.2 Define tonicity.

Osmolality describes the concentration of solutes in a solution. It is defined as the number of solute particles per 1 kg of solvent, also known as an **osmole**, or a unit of osmotic concentration. Osmolarity refers to the number of solutes per 1 liter of solvent and provides valuable insight into how solutions will behave under different conditions, enabling the manipulation of their properties to achieve optimal changes within the body.

Osmolality

Osmolality is a measure of the concentration of solutes, such as sodium, glucose, and urea, in a solution; specifically, it refers to the number of particles per kilogram of solvent. It is commonly used to assess the osmotic pressure of body fluids, such as blood or urine, and can provide important information about the body's fluid and electrolyte balance including:

- **Hyperosmolality** refers to a condition in which the concentration of solutes in a solution, such as blood or urine, is higher than normal. This can be caused by various factors, such as dehydration, diabetes, and certain drugs. Hyperosmolality may have serious consequences, such as impairment of the cardiovascular and circulatory system, as well as neurologic signs and symptoms such as irritability, seizures, and, in severe cases, coma.
- **Hypoosmolality** refers to a state in which the concentration of solutes in a solution is lower than normal. This can be caused by a variety of factors, including excessive water intake, certain drugs, disorders affecting the kidneys, and hormonal dysregulation of water balance. Hypoosmolality can have serious consequences, including neurologic signs and symptoms and even coma if not corrected.

- **Iso-osmolality** occurs when the concentration of solute particles per unit of volume in a solution is equal to a standard reference value.

Tonicity

Although osmolality and **tonicity** are related, they are not the same. Tonicity refers to the ability of a solution to cause a cell to gain or lose water and is relative to the cytoplasm of a cell (Khan & Farhana, 2023; Maldonado & Mohiuddin, 2022). A change in tonicity can have significant effects on cell function and overall fluid and electrolyte balance within the body, such as:

- **Hypertonicity** occurs when the tonicity of a solution is greater than that of the cytoplasm of a cell. This state can cause water to move out of the cell, potentially leading to cell shrinkage and changes in cell function. Hypertonicity can be caused by a variety of factors, including dehydration and increased solute concentration in a solution, such as with high glucose levels in the blood.
- **Hypotonicity** is related to hypoosmolality. It is a state in which the tonicity of a solution is less than that of the cytoplasm of a cell. Water can then move into the cell, potentially leading to swelling and other changes in cell function. Hypotonicity can be caused by a variety of factors, including excessive water intake and certain medical conditions.
- **Isotonicity** exists when the tonicity of a solution is equal to that of the cytoplasm of a cell. This means the concentration of solutes in the solution is balanced with the concentration of solutes inside the cell, resulting in no net movement of water into or out of the cell.

4.3 Maintaining Homeostasis

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 4.3.1 Describe how the body maintains homeostasis.
- 4.3.2 List factors that affect the body's homeostasis.
- 4.3.3 Discuss osmotic equilibrium and transient changes.

Most medical conditions can be attributed to a breakdown in the homeostatic control system, whether it is due to an inability to detect external changes, failure to initiate a feedback loop, inability to respond to or return to the set point, or failure in the set point itself. The primary objective of health care providers is to restore the body's homeostasis to prevent cellular death and irreversible organ damage.

Maintaining Homeostasis

The human body maintains a state of internal balance, called homeostasis, that is regulated at the cellular level. Even when the external environment fluctuates, the body strives to keep this balance within a narrow range. However, a temporary transient change can occur before the body returns to a steady state. Changes in the extracellular or intracellular fluid compartments can occur due to internal or external factors and are crucial for maintaining a narrow range to prevent cell death, tissue damage, and organ dysfunction (Libretti & Puckett, 2023).

Factors Impacting Homeostasis

Disturbances in physiologic factors can have a significant impact on the body's ability to maintain homeostasis. Such disturbances include:

- Disruptions in energy and nutrient balance, such as those that cause fluctuations in glucose levels
- Dysregulation of immune response modulators, such as pH and cortisol
- Disturbances in fluid and electrolyte levels, particularly sodium, potassium, and calcium

These components play a critical role in maintaining homeostasis and are governed by a complex **homeostatic mechanism** called a feedback loop, which is discussed in more depth in a later section of this chapter.

Osmotic Equilibrium

Osmotic equilibrium occurs when the concentration of solutes on either side of a **semipermeable membrane** is equalized. It is achieved when the osmotic pressure of a solution is equal to the **hydrostatic pressure** on the solution. The force that causes the reabsorption of fluid from the interstitial fluid into the capillaries is known as

osmotic pressure or oncotic pressure. Unlike hydrostatic pressure, which pushes fluid out of the capillaries, osmotic pressure pulls fluid back into them. This balance ensures that the optimal concentrations of electrolytes and nonelectrolytes are maintained in cells, body tissues, and interstitial fluid. Transient changes in the body, such as changes in temperature or pH, can disrupt the osmotic equilibrium, leading to a shift of water and solutes between intracellular and extracellular fluid compartments in an attempt to restore balance.

The **Na^+K^+ATPase pump** (also referred to as the sodium-potassium-ATPase pump) is an essential component in maintaining osmotic equilibrium (Pirahanchi et al., 2023). This pump moves sodium ions out of the cell and potassium ions into the cell, against their concentration gradients. This active transport process requires energy from **adenosine 5-triphosphate (ATP)**, an energy molecule (Hoorm et al., 2020). Osmotic equilibrium is essential for maintaining proper functioning of cells and body tissues. Figure 4.5 illustrates the Na^+K^+ATPase pump and the method by which it allows for osmotic equilibrium.

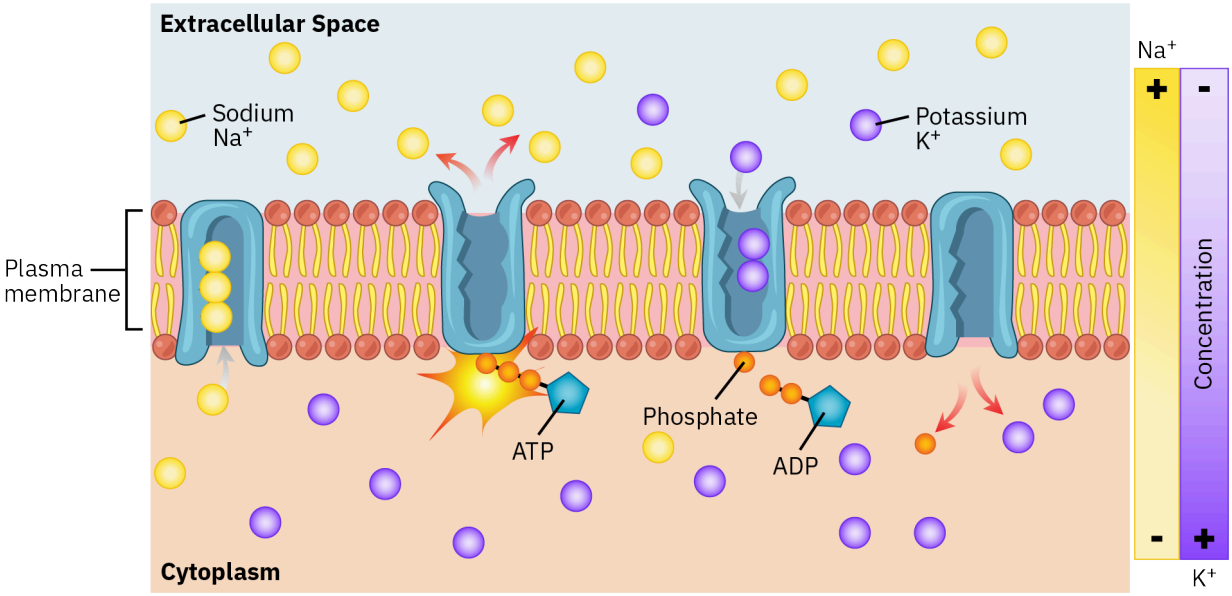


FIGURE 4.5 The Na^+K^+ATPase pump maintains osmotic equilibrium by moving sodium and potassium ions. (credit: modification of work from *Anatomy and Physiology 2e.* attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

4.4 Negative Feedback Loop

LEARNING OUTCOMES

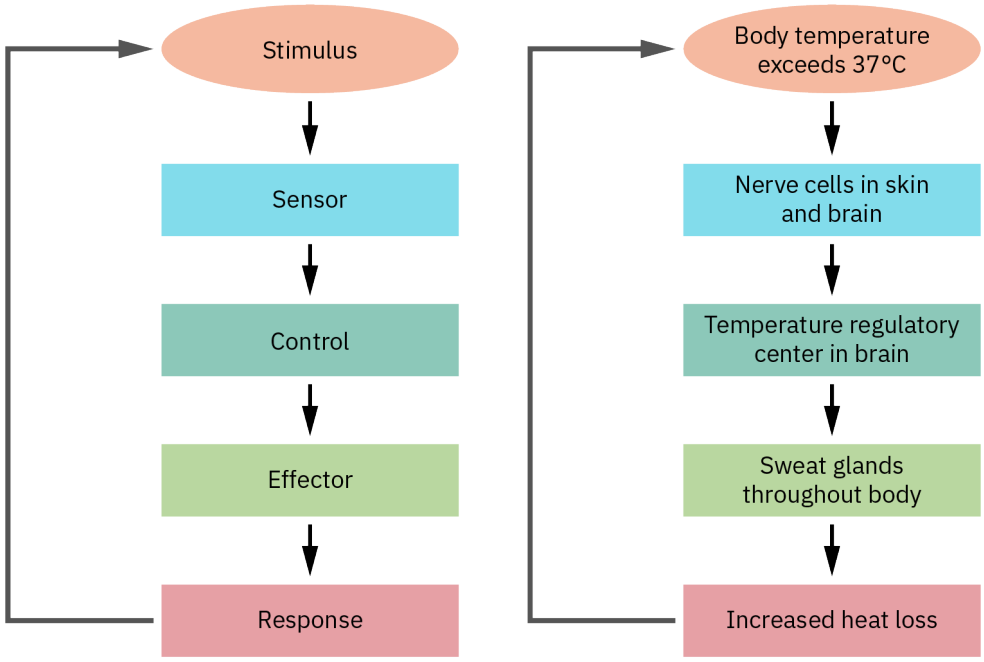
By the end of this section, you should be able to:

- 4.4.1 Define negative feedback loops as they relate to homeostasis.
- 4.4.2 Describe homeostatic responses within the body.
- 4.4.3 Explain positive feedback.

Feedback loops provide a mechanism for the body to maintain homeostasis. Feedback loops include **negative feedback**, the **homeostatic response system**, and **positive feedback**.

Negative Feedback and Homeostasis

Negative feedback is critical in regulating the body's homeostasis to promote optimal health and well-being. These inhibitory loops allow the body to self-regulate by counteracting any deviation from normal conditions. The process begins with an increase in output from a body system, leading to higher levels of specific proteins or hormones. This increase subsequently triggers the homeostatic response system to inhibit or reverse the production of those proteins or hormones, preventing their levels from rising further. The body thus reduces the number of these proteins or hormones, maintaining a balance within the normal physiologic limits (Chakravarty et al., 2023; Molnar & Gair, n.d.). An example of negative feedback within the body is depicted in Figure 4.6.



(a) Negative feedback loop (b) Body temperature regulation

FIGURE 4.6 A negative feedback loop regulates body temperature. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Homeostatic Response System

The homeostatic response system is a biological structure that is in a constant state of flux because of external and internal factors that push the body's systems away from equilibrium. The homeostatic response system is vital for maintaining a stable internal environment. When the body experiences a stimulus, such as an elevated body temperature, a neuron (nerve cell) within the brain acts as a receptor or sensor, relaying the message to the control center, which may be the hypothalamus, pituitary gland, or nervous system. The control center then activates effectors, whose role is to counteract the stimulus, thereby restoring homeostasis (see Figure 4.6) (Libretti & Puckett, 2023). In this way, the homeostatic response system enables the body to adjust to changing conditions and maintain stability.

Positive Feedback

In positive feedback, the body responds to a stimulus by amplifying or enhancing it rather than inhibiting it. This mechanism leads to a continuous increase in the stimulus, also known as a runaway effect, creating a self-reinforcing cycle. Positive feedback loops are commonly found in processes that require rapid and decisive responses, such as:

- Blood clotting
  - When an injury occurs, platelets in the blood stick to the damaged area and release chemical signals that attract more platelets. This recruitment of platelets leads to the formation of a blood clot, which further activates more platelets and reinforces the clotting process.
- Lactation
  - During lactation, the mechanical stimulation of nerve endings in the breast signals the posterior pituitary gland to release oxytocin, which stimulates the contraction of myoepithelial cells within the breast. As breast milk is released, the sucking action of the infant continues, and this further stimulates the nerve endings in the breast, creating a positive feedback loop.
- Uterine contraction during childbirth
  - During childbirth, the pressure of the newborn against the cervix and the tissue of the pelvic floor causes contraction of the uterus, which then results in the release of oxytocin, which stimulates stronger contractions. As contractions intensify, more oxytocin is released, resulting in positive feedback until the

infant is delivered (Libretti & Puckett, 2023).

Nonetheless, when not properly regulated, positive feedback loops may give rise to instability and potentially adverse consequences.

LINK TO LEARNING

Homeostasis: The Negative and Positive Feedback Loops

Access multimedia content (https://openstax.org/books/pharmacology/pages/4-4-negative-feedback-loop)
In this video, Dr. Mike Todorovic, senior lecturer of anatomy and physiology at Griffith University, Queensland, Australia, discusses the importance of homeostasis and explains the negative and positive feedback loops.

Chapter Summary

This chapter gave an overview of homeostasis, the body's ability to maintain a stable internal environment despite changes in the internal and external environments. One important component of homeostasis is the regulation of osmolality, which refers to the balance of solutes and water in the body. Homeostatic equilibrium is maintained through negative feedback loops, which involve a stimulus, a control center, and an effector, and positive feedback loops, which amplify a signal and can lead to a runaway effect if uncontrolled. The body's ability to maintain homeostasis is essential for proper functioning of cells and tissues.

Key Terms

active transport the process of moving molecules across a cellular membrane through the use of cellular energy
adenosine 5-triphosphate (ATP) a coenzyme that works with enzymes to transfer energy by releasing phosphate groups
anions negatively charged ions
cations positively charged ions
cytoplasm fluid inside a cell but outside the nucleus
effector an organ or tissue that receives information from the control center and acts to bring about the changes needed for homeostasis
extracellular fluid the fluid that surrounds the cells of the body
feedback loop a part of homeostasis that provides a mechanism for the body to maintain stability
homeostasis a state of balance
homeostatic mechanism a process that maintains the stability of the internal environment in response to fluctuations to external environmental conditions
homeostatic response system a self-regulating process in which the body maintains stability
hydrostatic pressure the pressure that any fluid in a confined space exerts
hyperosmolality a condition in which the concentration of solutes in a solution is higher than normal
hypertonicity a condition in which the tonicity of a solution is higher than that of the cytoplasm of a cell
hypoosmolality a state in which the concentration of solutes in a solution is lower than normal
hypotonicity a state in which the tonicity of a solution is lower than that of the cytoplasm of a cell
interstitial compartment fluid that surrounds tissue cells
intracellular fluid fluid that is contained within the cells of the body
intravascular compartment fluid inside the blood cells and plasma
ions atoms or groups of atoms that have one or more positive or negative electrical charges
iso-osmolality a state in which the concentration of solutes in a solution is equal
isotonicity a state in which the tonicity of a solution is equal to that of the cytoplasm of a cell
Na^+K^+ATPase pump a protein pump that acts to transport sodium and potassium ions across the cell membrane by using adenosine 5-triphosphate (ATP)
negative feedback a homeostatic process that counteracts a change, bringing the parameter back toward its set point
osmolality the number of solute particles per kilogram of solvent
osmole a unit of osmotic concentration
osmosis the movement of water molecules from a solution with a high concentration of water molecules to a solution with a lower concentration of water molecules, through a cell's semipermeable membrane
osmotic equilibrium a state when the concentration of a solute in water is the same on both sides of a semipermeable membrane
osmotic pressure the minimum pressure that must be applied to a solution to halt the flow of solvent molecules through a semipermeable membrane
positive feedback feedback that amplifies or magnifies a change
receptor part of the homeostatic system that receives information regarding balance within the body
semipermeable membrane a membrane that allows certain molecules or ions to pass through it by diffusion or active transport
solutes dissolved substances
tonicity the ability of a solution to cause a cell to gain or lose water; it is relative to the cytoplasm of a cell
transcellular compartment a small volume of fluid that is contained within certain body cavities and structures, also known as third space
transient change a temporary change that can occur before the body returns to a steady state of homeostasis

Review Questions

1. A nurse is preparing to teach a client about temperature regulation and homeostasis. Which statement should the nurse include in the teaching plan?
    a. Homeostasis makes your blood pressure rise when you experience stress.
    b. Homeostasis allows you to maintain a stable body temperature despite the outside temperature.
    c. Homeostasis is solely under the control of your brain and nervous system.
    d. Homeostasis converts food into energy.

2. The nurse is caring for a client with a high serum osmolality. Which condition is the client likely to have?
    a. Dehydration
    b. Fluid volume excess
    c. Hypothermia
    d. Hyperkalemia

3. The nurse is caring for a client with excessive fluid accumulation in the pleural cavity. The nurse determines that fluid is accumulating in which fluid compartment?
    a. Intracellular
    b. Extracellular
    c. Interstitial
    d. Transcellular

4. The nurse is caring for a client who has been experiencing diarrhea. Which anion does the nurse anticipate the client is losing through this loss of extracellular fluid?
    a. Calcium
    b. Sodium
    c. Potassium
    d. Chloride

5. The nurse is caring for a client with a gastrointestinal hemorrhage. Which fluid compartment does the nurse understand is losing fluid?
    a. Interstitial compartment
    b. Intravascular compartment
    c. Transcellular compartment
    d. Intracellular compartment

6. A nurse is caring for a pregnant client who is in labor. Which of the following statements accurately describes the concept of positive feedback in the context of labor?
    a. Oxytocin is suppressed, stimulating uterine contractions.
    b. Oxytocin is released, stimulating uterine contractions.
    c. Oxytocin is suppressed, increasing contractions.
    d. Oxytocin is released, halting uterine contractions.

7. A nurse is teaching a group of nursing students about the Na^+K^+ATPase pump. Which of the following statements accurately describes the role of this pump in maintaining cellular function?
    a. Potassium moves out of the cell and sodium moves into the cell, thereby maintaining a higher concentration of potassium inside the cell.
    b. Sodium moves out of the cell and potassium moves into the cell, thereby maintaining a higher concentration of sodium inside the cell.
    c. Sodium and potassium move out of the cell, thereby maintaining an equal concentration of electrolytes inside and outside the cell.
    d. Sodium and potassium move into the cell, thereby maintaining a higher concentration of electrolytes outside the cell.

8. Which of the following is an example of a negative feedback loop in the human body?
   a. Release of oxytocin during childbirth
   b. Blood clotting
   c. Lactation
   d. Regulation of blood glucose levels

9. The nurse is caring for a client with a fluid imbalance. Which statement accurately describes the distribution of intracellular (ICF) and extracellular fluid (ECF) in the body?
   a. The ICF constitutes approximately 40% of total body fluid, and ECF accounts for 20%.
   b. The ICF constitutes approximately 40% of total body fluid, and ECF accounts for 60%.
   c. The ICF constitutes approximately 20% of total body fluid, and ECF accounts for 80%.
   d. The ICF constitutes approximately 80% of total body fluid, and ECF accounts for 20%.

10. Which of the following best describes the concept of osmotic equilibrium in the body?
   a. The balance of water and electrolytes in the body
   b. The balance of water and solutes across a semipermeable membrane
   c. The balance of ions in the body's extracellular and intracellular fluid compartments
   d. The balance of acids and bases in the body's fluid

CHAPTER 5

Fluids and Electrolytes, Vitamins, Minerals, and Alternative Therapies

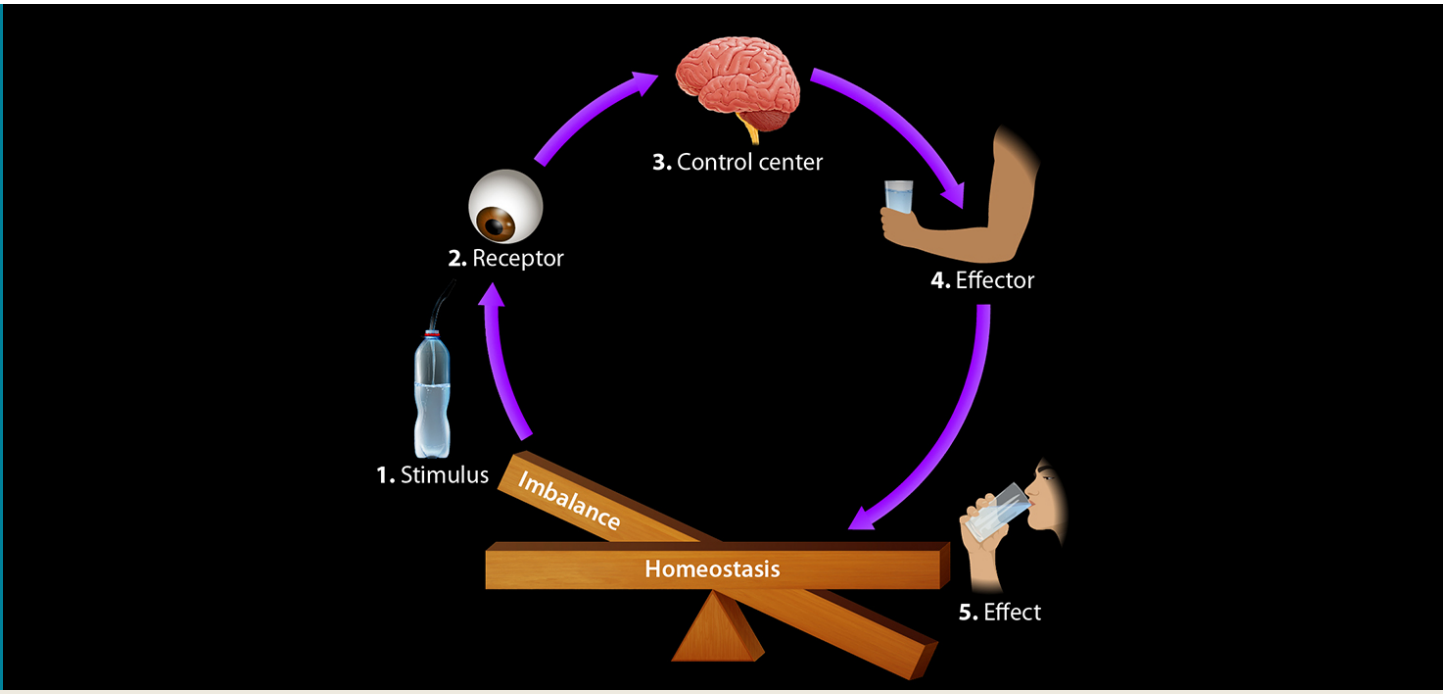


FIGURE 5.1 The nervous system sends chemical and electrical messages between the brain and other parts of the body to control homeostasis (a state of stable equilibrium between physiological processes), physical reflexes, and both voluntary and involuntary activities. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Maintaining a healthy balance of fluids, electrolytes, vitamins, and minerals is a crucial aspect of a person's overall well-being. Traditional pharmacological interventions are often used to manage imbalances in these areas. However, alternative therapies may also offer potential benefits to relieving symptoms and conditions caused by an imbalance in these areas. Understanding the role of fluids and electrolytes, as well as the potential uses and limitations of alternative therapies, is important for health care providers seeking to optimize their clients' health and well-being.

5.1 Fluid Volume

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 5.1.1 Define fluid volume.
- 5.1.2 Discuss the process of fluid volume deficit and excess as it relates to the body.
- 5.1.3 Describe cellular compartments and their role in fluid balance.
- 5.1.4 Explain the importance of blood and blood products.

Fluid volume is a critical component of the body's homeostasis, allowing for proper functioning of numerous

physiological processes. Disruptions to fluid volume can occur due to a variety of factors and can have serious consequences if left untreated. Maintaining an appropriate balance of fluids and electrolytes is essential for optimal health.

Fluid Volume Introduction

Fluid volume refers to the total amount of fluid present in the body, which includes both intracellular (inside cells) and extracellular (outside cells) fluids. The body is composed of approximately 60 percent water, which is distributed throughout the body in various compartments, including blood vessels, tissues, and organs.

The fluid volume in the body is tightly regulated through a complex system of feedback mechanisms that help to maintain a balance of fluids and electrolytes. These mechanisms, which are discussed in Introduction to Homeostasis, help to ensure that the body's cells receive the appropriate amount of nutrients and oxygen and that waste products are removed efficiently. Figure 5.2 shows how diffusion works across cell membranes to create a balance.

Maintaining, monitoring, and regulating fluid volume in the body is essential for proper bodily functions and an important aspect of medical care, especially when looking at fluid imbalances, which will be discussed in the next section.

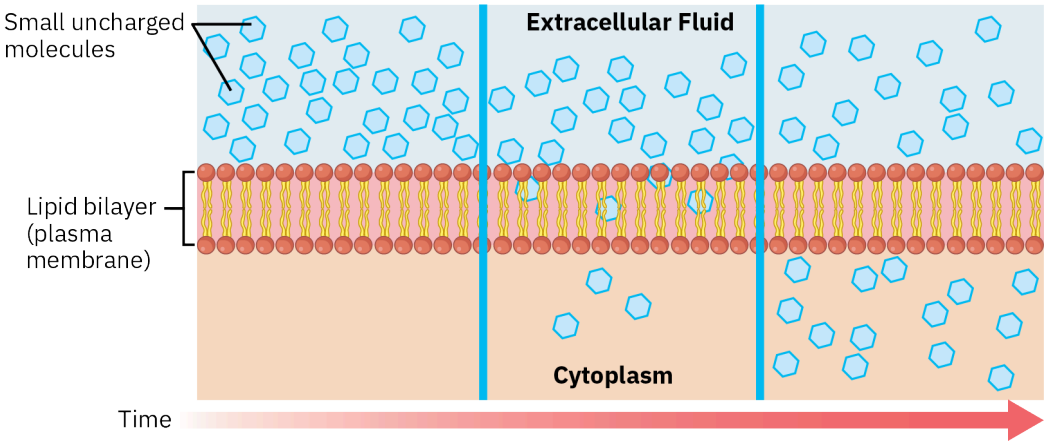


FIGURE 5.2 The structure of the lipid bilayer allows substances, such as oxygen and carbon dioxide, and molecules, such as lipids, to pass through the cell membrane by simple diffusion. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Fluid Imbalances

A fluid imbalance occurs when there is an abnormal distribution of fluids between the **intracellular fluid** (ICF) and the **extracellular fluid** (ECF) compartments within the body. An abnormal distribution of fluids between the ICF and ECF compartments can disrupt cellular function and result in fluid imbalance in the form of either a deficit or an excess (Brinkman et al., 2023). These fluid imbalances will be discussed in more detail in the subsequent sections.

A fluid imbalance can be caused by a variety of factors including medical conditions, such as kidney and heart disease, medication use, and lifestyle factors, such as diet and exercise.

Treatment for the imbalance typically involves addressing the underlying cause and restoring the balance of fluids and electrolytes in the body. This may include oral or intravenous fluids, electrolyte replacement, and other interventions as necessary.

Fluid Volume Deficit

Fluid volume deficit, also known as **hypovolemia**, is a condition that occurs when there is a decrease in the body's fluid volume. This can be due to a loss of sodium from the body, decreased fluid intake, or a combination of both. Several conditions and diseases can lead to fluid volume deficit, such as dehydration, diabetes insipidus, and hemorrhage. Certain drugs, including diuretics, blood pressure drugs (e.g., angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs), which inhibit aldosterone), and laxatives (which increase fluid loss through stools), can lead to hypovolemia (Melendez-Rivera & Anjum, 2022).

Manifestations of fluid volume deficit include:

- Postural dizziness
- Fatigue
- Confusion
- Muscle cramps
- Chest pain
- Abdominal pain
- Postural hypotension
- Tachycardia

The diagnosis of fluid volume deficit involves a comprehensive approach that includes a thorough physical examination, a detailed client history, and laboratory tests such blood chemistry panels, electrolyte panels, complete blood cell counts, and urinalysis.

Treatment of fluid volume deficit involves replenishing fluids and electrolytes through oral rehydration therapy or intravenous (IV) fluid replacement, depending on the severity of the deficit.

Fluid Volume Excess

Fluid volume excess, also known as **hypervolemia**, is a condition that occurs when there is an abnormal increase in the body's total fluid volume. This can be due to increased fluid intake, decreased fluid output, or a combination of both. Several conditions and diseases can lead to fluid volume excess, including heart failure, liver disease, and kidney disease (Ekinci et al., 2018). Certain drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids (which can lead to fluid retention by affecting the kidneys' ability to eliminate sodium and water), hormonal therapies such as estrogen replacement (which can lead to fluid retention), and diabetes drugs such as thiazolidinediones can cause fluid retention as an adverse effect.

Manifestations of fluid volume excess include:

- Shortness of breath
- Crackles in the lungs
- Swelling in the legs, ankles, and feet
- Weight gain
- High blood pressure
- Fatigue

To diagnose fluid volume excess, the provider must take a comprehensive approach. This involves a physical examination, a detailed client history, and various laboratory tests such as blood chemistry panels, electrolyte panels, complete blood cell counts, and urinalysis. Additionally, imaging studies like a chest x-ray and echocardiogram may also be necessary to assess the heart and lungs.

Treatment of hypervolemia involves addressing the underlying cause, restricting fluid and sodium intake, and increasing urine output through diuretic drugs. In severe cases, hospitalization may be required for monitoring and treatment.

Fluid Replacement

Fluid volume replacement is a medical treatment that involves replenishing lost fluid and electrolytes, specifically sodium in the body, typically through IV infusion. This treatment is commonly used to address fluid volume deficit and conditions that result in body fluid loss.

Fluid volume replacement works by restoring the balance of fluid and electrolytes that are essential for maintaining proper bodily function. Electrolytes are electrically charged minerals such as sodium, potassium, chloride, phosphate, magnesium, and calcium, which play roles in regulating cellular function and maintaining the body's fluid balance (Melendez-Rivera & Anjum, 2022).

Fluid volume replacement usually involves various types of fluids or a combination of fluids containing electrolytes and other nutrients. The specific type of fluid used depends on the client's condition and individual needs. Fluid replacement and types of intravenous fluid replacement solutions will be discussed in more detail in subsequent

sections.

Fluid volume replacement is administered by health care professionals, and the treatment is closely monitored to ensure that the client's fluid and electrolyte levels are being properly balanced.

Blood and Blood Products

Blood is a vital component of fluid balance. Blood circulates through the body and is composed of various cells including red blood cells, white blood cells, and platelets (see Figure 5.3), as well as a liquid component called plasma. Blood plays an important role in:

- *Oxygen transport:* Blood transports oxygen from the lungs to the body's tissues. Red blood cells contain hemoglobin, which binds with oxygen and carries it throughout the body.
- *Nutrient transport:* Blood carries nutrients such as glucose, amino acids, and fatty acids to the body's cells, where they are used for energy and cellular function.
- *Waste removal:* Blood transports waste products such as carbon dioxide to the lungs and urea to the kidneys, where they are removed from the body.
- *Immune defense:* White blood cells play a crucial role in the body's immune system, defending against infections and diseases.
- *Blood clotting:* Blood contains platelets and clotting factors that help stop bleeding and promote the healing of injured tissues.
- *Hormone regulation:* Blood helps regulate hormone levels in the body, which controls many important functions such as metabolism, growth, and development.

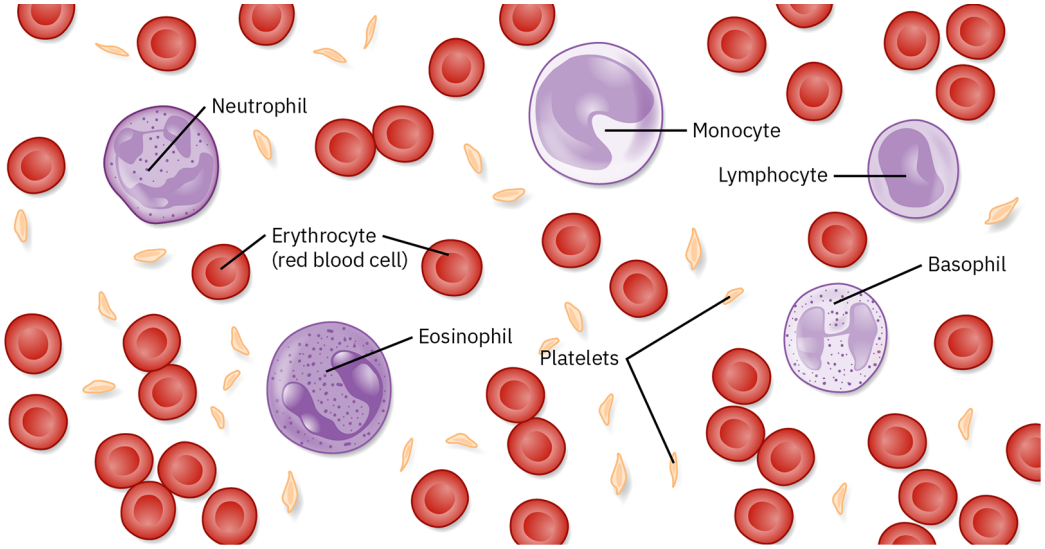


FIGURE 5.3 White blood cells (including basophils, eosinophils, lymphocytes, monocytes, and neutrophils), red blood cells, and platelet blood components are shown in this diagram. (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Blood products are derived from donated human blood and are used for a variety of medical purposes, including fluid volume replacement. The most commonly used forms of blood products for fluid replacement are packed red blood cells (PRBCs), platelets, plasma, and cryoprecipitated anti-hemophilic factor (cryo) (American Red Cross, n.d.).

When a person experiences severe blood loss or fluid volume deficit, fluid volume replacement is necessary to restore their blood volumes and prevent **shock**. Blood and blood products are administered intravenously to replenish lost fluids/blood, maintain the body's blood pressure and hormonal balance, and restore the body's oxygen-carrying capacity (Lotterman & Sharma, 2022). Blood and blood products will be discussed in more depth in the next section of this chapter.

5.2 Electrolytes

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 5.2.1 Define electrolytes.
- 5.2.2 Discuss the functions of major electrolytes.
- 5.2.3 Describe clinical manifestations related to common electrolyte imbalances.
- 5.2.4 Identify characteristics of treatment for common electrolyte imbalances.
- 5.2.5 Explain the indications, actions, adverse reactions, contraindications, and interactions of electrolyte therapy.
- 5.2.6 Describe the nursing implications related to treatment of electrolyte imbalances.
- 5.2.7 Explain the client education related to treatment of electrolyte imbalances.

Electrolytes are minerals that carry electrical charges and play vital roles in maintaining fluid homeostasis and regulating various physiological functions. When there are imbalances in electrolytes, it can lead to a range of symptoms and health issues that can significantly impact an individual's health and well-being. Therefore, it is important to maintain proper electrolyte balance through a healthy diet, hydration, and medical care.

Electrolytes

Electrolytes are found in ICF and ECF compartments. They are responsible for many functions including regulating nerves, muscle function, and fluid balance within the body and helping to maintain a healthy pH level. In the next few sections, you will learn about potassium, sodium, calcium, phosphorus, magnesium, and chloride.

Potassium

Potassium (K) is an essential cation primarily found inside cells. The normal intracellular concentration of potassium ions in the body is approximately 140 mEq/L; the normal extracellular concentration is around 4 mEq/L. Therapeutic serum potassium levels are 3.6 to 5.4 mEq/L (Shrimanker & Bhattarai, 2023).

Potassium moves into and out of the cells via the **sodium-potassium-ATPase pump** (also known as the Na^+K^+ATPase pump) (see Figure 5.4), which uses energy from ATP hydrolysis to transport sodium ions out of cells and potassium ions into cells against their concentration gradients. The pump is vital for maintaining the concentration gradient of sodium and potassium ions across the cell membrane (Shrimanker & Bhattarai, 2023).

The levels of potassium in the body are influenced by acid–base imbalances. Acidotic conditions can lead to the movement of potassium out of cells, whereas alkalotic conditions can promote movement of potassium into cells. There is an inverse relationship between sodium and potassium reabsorption in the kidneys. Additionally, the hormone aldosterone plays a role in regulating potassium excretion (Shrimanker & Bhattarai, 2023).

Potassium is necessary for transmission and conduction of nerve impulses and for contraction of skeletal, cardiac, and smooth muscles. It is essential for normal renal function and **glycolysis**, the process of converting glucose into energy. Potassium also promotes glycogen storage in hepatic cells and regulates osmolality of cellular fluids (Dalga et al., 2023; Shrimanker & Bhattarai, 2023).

Hyperkalemia

Hyperkalemia is a condition where the level of potassium in the blood is higher than normal (usually above 5.5 mEq/L) (Shrimanker & Bhattarai, 2023). Common causes include excessive potassium intake, impaired kidney function that decreases its excretion, or a shift from intracellular to extracellular spaces.

Manifestations of hyperkalemia include muscle weakness, fatigue, palpitations, tachycardia, paresthesia, nausea, diarrhea, and confusion. Electrocardiogram (ECG, EKG) changes such as peaked T waves, flattened P waves, and prolonged QRS durations may be seen. In severe cases, hyperkalemia can cause cardiac arrest (Shrimanker & Bhattarai, 2023).

Treatment for hyperkalemia includes removing excess potassium from the body through dialysis, administering drugs that shift potassium from the extracellular fluid into the cells, administering potassium-binding drugs that help bind to potassium and excrete it from the body, and treating the underlying cause. Common underlying causes of hyperkalemia include kidney failure and diabetes (Shrimanker & Bhattarai, 2023).

Nursing implications include restricting potassium in the diet. The health care provider may order administration of sodium bicarbonate (which elevates the pH level and moves potassium back into cells, thereby lowering the serum potassium levels), insulin and glucose (insulin helps to move potassium back into the cells by promoting the uptake of glucose and potassium), and/or sodium polystyrene sulfonate (which exchanges sodium ions for potassium ions in the colon, leading to removal of excess potassium through the stool). Monitoring potassium levels and reporting significant changes to the health care provider is key in ensuring appropriate potassium balance within the body (Shrimanker & Bhattarai, 2023).

Clients should avoid food high in potassium (such as bananas, potatoes, and spinach), avoid salt substitutes (as these are high in potassium), take drugs as prescribed, and seek medical attention if they develop manifestations of hyperkalemia, such as palpitations, tachycardia, and muscle weakness.

Hypokalemia

Hypokalemia is a condition where the level of potassium in the blood is lower than normal (less than 3.6 mEq/L). Hypokalemia can be caused by excessive loss of potassium through the kidneys, increased loss of potassium in the digestive tract (through vomiting or diarrhea), insufficient potassium intake, redistribution of potassium from extracellular fluid into cells (by insulin therapy, alkalosis, or drugs), or by a magnesium deficiency (magnesium is necessary for the proper function of channels that regulate potassium transport in cells) (Shrimanker & Bhattarai, 2023).

Manifestations of hypokalemia include fatigue, muscle weakness, muscle cramps, constipation, and irregular heartbeat. EKG changes may be present with T wave inversion, widespread ST depression, and prominent U waves (Shrimanker & Bhattarai, 2023).

Treatment for hypokalemia includes administering potassium supplements orally or intravenously, treating the underlying cause, and monitoring for complications such as low blood pressure. Common underlying causes of hypokalemia include diarrhea, diuretic use, excessive laxative use, excessive sweating, and diabetic ketoacidosis. Adverse reactions with potassium supplements include nausea, vomiting, abdominal pain, and diarrhea. Potassium supplements should be used cautiously with ARBs, ACE inhibitors, and potassium-sparing diuretics such as spironolactone.

Nursing implications include monitoring potassium levels, assessing for manifestations of hypokalemia, and administering potassium supplements as prescribed by the health care provider. Clients should eat a diet containing potassium-rich foods (such as bananas, lentils, and dried fruits). Clients should avoid excessive use of laxatives or diuretics and report symptoms of hypokalemia, such as muscle weakness and constipation, to their health care provider.

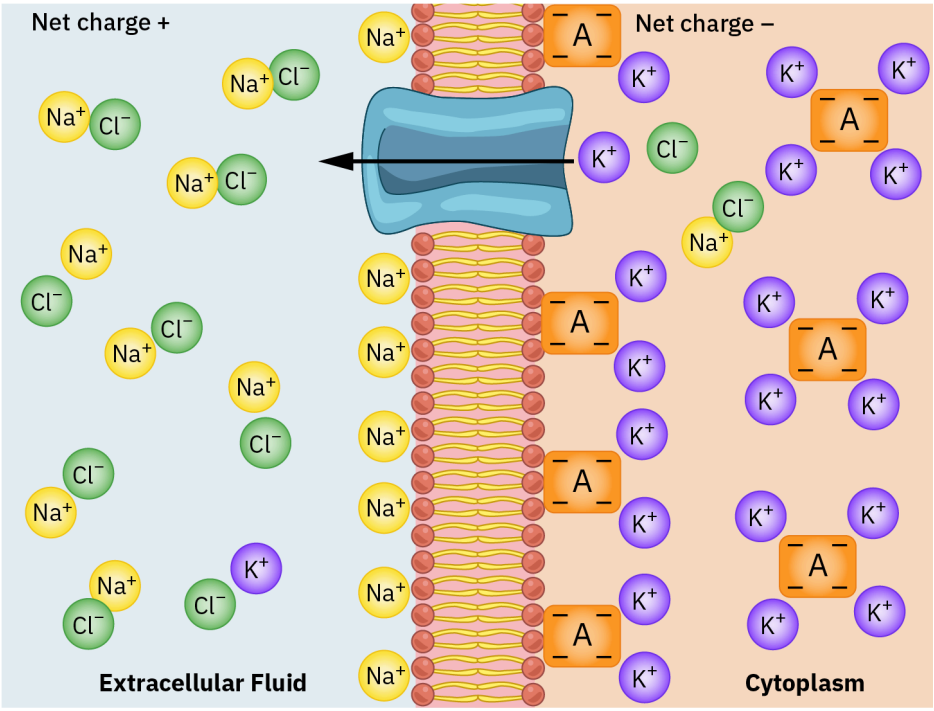


FIGURE 5.4 The sodium-potassium-ATPase pump expends ATP energy to extrude sodium ions out of cells and usher potassium ions into cells. (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC by 4.0 license)

SAFETY ALERT

Potassium and IV Bolus or Push

Never push or bolus potassium intravenously. Rapid administration of potassium via intravenous bolus or push can result in cardiac dysrhythmias and client death. Intravenous potassium solutions are often premixed (diluted in 100–1000 mL of normal saline or lactated Ringer's solutions) to decrease the risk of errors.

CLINICAL TIP

Potassium Administration and IV Site Assessment

Monitor the client's IV site closely when administering potassium intravenously for infiltration because potassium solutions can cause extravasation and tissue necrosis if they infiltrate into subcutaneous tissues. Discontinue the IV fluids immediately if this occurs and notify the health care provider. Maximum potassium concentration is 40 mEq/L with a maximum peripheral infusion rate of 20 mEq/hour (Sur & Mohiuddin, 2022).

Sodium

Sodium (Na) is predominantly an extracellular cation, meaning it is found primarily outside of the cells in the extracellular fluid. The normal concentration of sodium in the body is approximately 135–145 mEq/L (which is the same as the therapeutic range for serum sodium levels), whereas the normal intracellular concentration is around 10 mEq/L (Shrimanker & Bhattarai, 2023).

The sodium-potassium-ATPase pump is vital for maintaining the concentration gradient of sodium and potassium ions across the cell membrane. As you may recall, the pump uses energy to move sodium out of cells and potassium into cells against their concentration gradients in order to maintain sodium–potassium balance (Shrimanker & Bhattarai, 2023).

Sodium has many functions within the body. It is the primary determinant of the osmolality and volume of extracellular fluids. It is involved in the transmission of nerve impulses throughout the body, including the brain and nervous system. Sodium is important for proper muscle contraction and relaxation. Potassium and sodium work

together to regulate blood pressure by maintaining the proper fluid balance. Sodium helps to maintain the pH balance of the blood. Additionally, sodium is necessary for the absorption of certain nutrients such as glucose and amino acids in the small intestine (Shrimanker & Bhattarai, 2023; Veniamakis et al., 2022).

Hypernatremia

Hypernatremia is a condition in which the sodium levels in the blood are higher than normal (above 145 mEq/L). As sodium levels rise, hypertonicity occurs, and water shifts out of the ICF space into the ECF. This can be caused by dehydration, excessive salt intake, deficient water intake, or kidney problems (Shrimanker & Bhattarai, 2023).

Manifestations of hypernatremia include thirst, dry mucous membranes, flushed dry skin, elevated body temperature, muscle twitching, seizure, and coma. Treatment for hypernatremia involves correcting the underlying cause and restoring fluid and electrolyte balance. Intravenous fluids and drugs to lower sodium levels may be administered gradually.

Nursing implications include monitoring intake and output as well as electrolyte levels. IV fluids and drugs such as diuretics are administered as needed.

CLIENT TEACHING GUIDELINES

The client with hypernatremia should:

- Avoid foods high in sodium, avoid using salt when cooking, and refrain from adding extra salt to foods at the table.
- Read food labels and over-the-counter (OTC) drug labels to avoid excessive sodium intake.
- Report manifestations of hypernatremia, such as thirst and muscle twitching, to their health care provider.

Hyponatremia

Hyponatremia is a condition in which sodium levels are lower than normal (less than 135 mEq/L). As sodium levels decrease, hypotonicity occurs, and water shifts from the ECF into the ICF. This can be caused by conditions such as kidney disease, heart failure, or excessive fluid intake (Shrimanker & Bhattarai, 2023). Manifestations of hyponatremia include muscle weakness, decreased deep tendon reflexes, headache, lethargy, confusion, weak or thready pulse, decreased blood pressure, seizures, and coma.

Treatment for hyponatremia includes correcting the underlying cause and restoring fluid and electrolyte balance. Oral sodium replacement or intravenous fluids may be necessary to restore homeostasis. Adverse reactions include hypertension and fluid volume excess. Sodium replacement supplements should be used cautiously in clients with advanced renal disorders or heart failure.

Nursing implications include monitoring intake and output of sodium and electrolyte levels, administering oral sodium replacements or intravenous solutions as ordered by the health care provider, and client education on fluid intake.

CLIENT TEACHING GUIDELINES

The client with hyponatremia should:

- Limit fluid intake to maintain proper fluid and electrolyte balance.
- Report manifestations or changes in symptoms such as headache and lethargy to the health care provider.

Calcium

Calcium (Ca) is the fifth most abundant mineral in the body and is present in both intracellular and extracellular fluid compartments. In the ECF, calcium is present in ionized and protein-bound forms; in ICF, calcium is primarily bound to proteins and organelles. The therapeutic range for serum calcium levels is 8.8–10.4 mg/dL (Drake & Gupta, 2022; Shrimanker & Bhattarai, 2023).

Calcium is necessary for the formation and maintenance of bones and teeth. It is also important for proper muscle

function, including contraction and relaxation. Calcium is involved in the transmission of nerve impulses and is necessary for the release of certain hormones and enzymes. Additionally, calcium is involved in the clotting of blood and helps to regulate heart rhythm (Shrimanker & Bhattarai, 2032). Calcium has an inverse relationship with phosphorus and a synergistic relationship with magnesium. The parathyroid hormone from the parathyroid gland and calcitonin from the thyroid gland regulate calcium levels. The absorption of calcium requires activated vitamin D.

Hypercalcemia

Hypercalcemia is a condition in which serum calcium levels are higher than normal (greater than 10.4 mg/dL). Hypercalcemia can be a result of hyperparathyroidism, malignancy, hypophosphatasia, and thiazide diuretic use (Drake & Gupta, 2022; Sadiq et al., 2022; Shrimanker & Bhattarai, 2023).

Manifestations of hypercalcemia include nausea, vomiting, loss of appetite, excessive thirst or urination, constipation, abdominal pain, bone pain, diminished deep tendon reflexes, confusion, kidney stones, muscle weakness or twitching, and an irregular heartbeat.

Treatment for hypercalcemia includes identifying and treating the underlying cause, such as hyperparathyroidism or certain cancers. Treatment options include drugs to decrease calcium levels, such as loop diuretics, bisphosphonates, or calcitonin, or IV fluids to help flush excess calcium from the body.

Nursing implications include close monitoring of calcium levels and vital signs, administering drugs as prescribed by the health care provider, and monitoring for complications such as kidney stones, renal impairment, and cardiac arrhythmias.

CLIENT TEACHING GUIDELINES

The client with hypercalcemia should:

- Avoid overuse of calcium-containing antacids.
- Report symptoms, such as bone pain or changes in urination, to the health care provider.

Hypocalcemia

Hypocalcemia is a condition in which serum calcium levels are lower than normal (lower than 8.8 mg/dL) (Drake & Gupta, 2022). Hypocalcemia can result from calcium loss from bone, pathologic fractures due to calcium loss, hypoparathyroidism, hyperphosphatemia, diarrhea, alcoholism, vitamin D deficiency, and malnutrition. Manifestations of hypocalcemia include paresthesia, muscle cramps or spasms, weakness, fatigue, difficulty swallowing or speaking, confusion, osteoporosis, irritability, seizures, and dysrhythmias (Shrimanker & Bhattarai, 2023).

Treatment for hypocalcemia includes identifying and treating the underlying cause, such as vitamin D deficiency. Treatment options may include calcium and vitamin D supplements, drugs to improve calcium absorption, or intravenous calcium if levels are severely low. Adverse reactions include constipation, severe diarrhea, and abdominal pain. Calcium supplements should be used cautiously with levothyroxine, tetracycline antibiotics, and quinolone antibiotics because they can decrease their absorption.

Nursing implications include administering oral or intravenous calcium supplements, administering vitamin D supplements, assessing renal and cardiac functioning, and monitoring the IV site for infiltration and extravasation.

CLIENT TEACHING GUIDELINES

The client with hypocalcemia should:

- Maintain a balanced diet with calcium-rich foods, such as dairy products enriched with vitamin D, sardines, salmon, winter squash, and edamame.

CLINICAL TIP

Calcium Supplements and Iron Administration

Avoid administering oral iron supplements within 1 to 2 hours of oral calcium supplements and dairy products because calcium may interfere with the absorption of iron and reduce its effectiveness (Piskin et al., 2022).

Phosphorous

Phosphorous (P) is the second most abundant element in the body and is a major anion in intracellular fluid. The majority of the body's phosphorus is found in phosphate; it is important to note that the terms phosphate and phosphorus are used interchangeably. Phosphorus is needed to help bones and teeth maintain their structure, for RNA and DNA synthesis, for cell signaling, and for pH balance in the body. The therapeutic range for serum phosphorus level is 3.4–4.5 mEq/L (Shrimanker & Bhattarai, 2023).

Hyperphosphatemia

Hyperphosphatemia is a condition where the body's phosphorus level is greater than the therapeutic range (above 4.5 mEq/L). Causes of hyperphosphatemia include chronic kidney disease, hypoparathyroidism, excess phosphorus intake, and certain drugs (Goyal & Jialal, 2022; Shrimanker & Bhattarai, 2023).

Manifestations of hyperphosphatemia include muscle spasms, hyperreflexia, nausea, diarrhea, and abdominal cramps. Treatment for hyperphosphatemia involves addressing the underlying cause and may involve restricting dietary intake of phosphorus, administering phosphate-binding drugs, and in severe cases, dialysis.

Nursing implications include monitoring serum phosphate levels, assessing manifestations, and educating the client regarding dietary intake.

CLIENT TEACHING GUIDELINES

The client with hyperphosphatemia should:

- Report symptoms such as abdominal pain and tetany to the health care provider.
- Avoid foods high in phosphorus, such as whole grains and nuts.

Hypophosphatemia

Hypophosphatemia is a condition where the body's phosphorus level is lower than the therapeutic range (below 2.5 mEq/L). Causes include malnutrition, alcoholism, hyperparathyroidism, and certain drugs, such as diuretics. Manifestations include muscle weakness, altered mental status, bone pain, paresthesia, and dysphagia (Sharma et al., 2022; Shrimanker & Bhattarai, 2023).

Treatment for hypophosphatemia depends on the underlying cause and may involve oral or intravenous phosphorus supplementation and adjusting drugs or drug dosages. Adverse effects of phosphorus supplements include kidney stones, headache, dizziness, and seizures. Phosphorus supplements should be used cautiously in clients at risk for kidney stones or who have kidney failure.

Nursing implications include monitoring phosphate levels, assessing manifestations for worsening symptoms, and monitoring for adverse effects of phosphorus supplements, which include bone pain, muscle cramps, confusion, tachycardia, or swelling in hands, legs, or feet.

CLIENT TEACHING GUIDELINES

The client with hypophosphatemia should:

- Report symptoms such as bone pain and tremors to the health care provider.
- Maintain a well-balanced diet with foods high in phosphorus, such as whole grain cereals, nuts, and dairy products.

- Drink a full glass of water every hour to reduce the risk of kidney stone development.

Magnesium

Magnesium (Mg) is a mineral that is essential for many physiological processes, including energy production, protein synthesis, muscle and nerve function, and bone health. It is found in both ICF and ECF. The therapeutic range for serum magnesium is 1.46–2.68 mEq/L (Shrimanker & Bhattarai, 2023). Magnesium assists in the release of parathyroid hormone (PTH). Magnesium and potassium have an interdependent relationship; when potassium levels decrease, so do magnesium levels, and vice versa.

Hypermagnesemia

Hypermagnesemia refers to high levels of magnesium in the blood (greater than 2.68 mEq/L). It can be caused by kidney dysfunction, excessive use of magnesium-containing antacids or laxatives, excessive magnesium supplement use, or use of certain medications, such as proton pump inhibitors and lithium-based psychotropic drugs (Cascella & Vaqar, 2023; Shrimanker & Bhattarai, 2023).

Manifestations of hypermagnesemia include weakness, lethargy, confusion, low blood pressure, and in severe cases, cardiac arrest. Treatment of hypermagnesemia consists of removing the cause of excess magnesium, administering drugs such as calcium gluconate to reduce magnesium in the body, and symptom management.

Nursing implications include close monitoring of electrolyte levels and timely reporting of any changes in client symptoms or laboratory values to the health care provider.

CLIENT TEACHING GUIDELINES

The client with hypermagnesemia should:

- Use magnesium or magnesium-containing supplements or drugs carefully.
- Promptly report any symptoms that may indicate hypermagnesemia, such as weakness and low blood pressure, to the health care provider.

Hypomagnesemia

Hypomagnesemia refers to low levels of magnesium in the blood (less than 1.46 mEq/L). It can be caused by a variety of factors including malnutrition, alcoholism, gastrointestinal disorders, and drugs such as diuretics. Manifestations include generalized weakness, tremors, cramps, arrhythmias, and seizures (Gragossian et al., 2022; Shrimanker & Bhattarai, 2023).

Treatment for hypomagnesemia involves oral or intravenous magnesium supplementation and addressing the underlying cause. Adverse reactions to magnesium supplements include nausea, abdominal cramping, diarrhea, hypotension, flushing of skin, and urinary retention. Magnesium supplements should be used cautiously in clients with diabetes, digestive disorders, and heart or kidney disorders.

Nursing implications involve careful monitoring of magnesium levels, identifying clients at risk for development of hypomagnesemia, and monitoring and reporting changes in symptoms and laboratory values to the health care provider.

CLIENT TEACHING GUIDELINES

The client with hypomagnesemia should:

- Take magnesium supplements with meals to prevent gastrointestinal upset and diarrhea.
- Eat foods rich in magnesium, such as avocado, broccoli, spinach, and lentils.

CLINICAL TIP

Magnesium and Folic Acid, Fiber, and Iron Supplements

Avoid administering magnesium within 2 hours of folic acid, fiber, and iron supplements because magnesium may interfere with the absorption of these drugs and reduce their effectiveness (National Health Service, 2023).

Chloride

Chloride (Cl) is an anion found primarily in the ECF and is essential in maintaining fluid balance and helping to regulate the pH of bodily fluids. Chloride ions are important for the formation of hydrochloric acid in the stomach, which is necessary for the digestion of food. Additionally, chloride ions work together with other electrolytes, such as sodium and potassium, to maintain proper electrical balance and conduct nerve impulses throughout the body. The therapeutic range for chloride is 98–106 mEq/L (Fishman, 2023; Shrimanker & Bhattarai, 2023).

Hyperchloremia

Hyperchloremia is a condition where there is an excess amount of chloride in the blood (greater than 106 mEq/L). It may be caused by various conditions such as dehydration, metabolic acidosis, and kidney disease and by certain drugs, such as chemotherapy (Shrimanker & Bhattarai, 2023).

Manifestations of hyperchloremia include weakness, confusion, lethargy, and tachypnea (rapid breathing). Treatment involves addressing the underlying cause in addition to fluid and electrolyte replacement.

Nursing implications include monitoring fluid and electrolyte balance, intake, and output; administering drugs such as diuretics as ordered; and maintaining the client on a low-sodium diet.

CLIENT TEACHING GUIDELINES

The client with hyperchloremia should:

- Avoid foods high in salt because chloride binds readily to sodium.
- Monitor their fluid intake and report symptoms of hyperchloremia, such as tachypnea and lethargy, to the health care provider.

Hypochloremia

Hypochloremia is a condition where there is a low amount of chloride in the blood (less than 98 mEq/L). It may be caused by diarrhea, vomiting, kidney disease, or metabolic alkalosis. Manifestations include weakness, fatigue, trouble breathing, and dizziness (Fishman, 2023; Shrimanker & Bhattarai, 2023).

Treatment is focused on treating the underlying cause, replacing fluids and electrolytes, and adjusting drugs or drug dosages. Adverse effects include fever and fluid volume excess. Fluid replacement with chloride-containing solutions should be administered cautiously in clients with heart failure and kidney disorders.

Nursing implications include monitoring intake and output, administering fluids and electrolytes per health care provider orders, and monitoring for signs of fluid volume excess, such as shortness of breath, crackles, and peripheral edema, from overtreatment.

CLIENT TEACHING GUIDELINES

The client with hypochloremia should:

- Maintain a balanced diet that includes sources of sodium.
- Report symptoms of hypochloremia, such as tremors and low blood pressure, to the health care provider.

5.3 Intravenous Fluid Therapy, Total Parenteral Nutrition, and Blood Products

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 5.3.1 Describe types of intravenous solutions.
- 5.3.2 Compare and contrast crystalloid and colloid intravenous solutions.
- 5.3.3 Define total parenteral nutrition and its uses.
- 5.3.4 Discuss the importance of blood and blood products in fluid balance.
- 5.3.5 Discuss how intravenous solutions are used to correct fluid imbalances within the body.

Fluid volume replacement is an important part of fluid and electrolyte homeostasis within the body. In this section of the chapter, intravenous fluid therapy, total parenteral nutrition, and blood products will be discussed.

Intravenous Fluid Therapy

Intravenous (IV) fluid therapy is a medical treatment that involves the administration of fluids directly into a person's veins through an intravenous catheter. The fluids are typically a combination of water, electrolytes, and other nutrients, depending on the specific needs of the client.

IV fluid therapy is used for a wide variety of medical conditions including hypovolemia, electrolyte imbalances, and shock. It is commonly used during and after surgical procedures to help maintain fluid balance and prevent complications.

A health care professional administers IV fluid therapy. The appropriate type and amount of fluid administered is based on the client's medical history, a thorough physical exam, and laboratory results. The fluids are delivered through an IV catheter, which is inserted into a peripheral vein or via a central venous access device or mediport. The rate and duration of IV fluid therapy will vary depending on the client's condition and response to treatment. Therapy may last a few hours, several days, or even weeks. Refer to Drug Administration for review of dosage calculation formulas for drops per minute and milliliters per hour as they relate to IV fluid therapy.

Overall, IV fluid therapy is critical in restoring fluid balance, maintaining blood pressure, and preventing complications related to fluid volume deficit. IV fluid therapy usually involves crystalloid solutions, colloid solutions, total parenteral nutrition, and blood and blood products, all of which will be discussed further in the following sections.

Crystalloid Solutions

Crystalloid solutions are a type of IV fluid therapy that consists of electrolytes and fluids that can readily cross the capillary walls. These solutions lack proteins that maintain **colloidal oncotic pressure** (osmotic pressure exerted by large proteins that holds water within the vascular space) that prevents water from leaving the intravascular space (Epstein & Waseem, 2022). These solutions are commonly used for short-term maintenance of fluids and in treating fluid volume deficits. The three main types of crystalloid solutions are isotonic, hypotonic, and hypertonic, which are discussed in the following sections; examples can be seen in Table 5.1.

Isotonic Solutions

Isotonic solutions have the same concentration of dissolved particles, such as sodium and glucose, as the body's own fluids. This means they have the same approximate osmolality as ECF or plasma. Because of their osmotic equilibrium, water does not enter or leave the cells. Isotonic solutions are typically used to treat conditions such as dehydration caused by vomiting, diarrhea, or excessive sweating or other conditions that cause fluid volume deficit (Epstein & Waseem, 2022).

Hypotonic Solutions

Hypotonic solutions have a lower concentration of dissolved particles than the body's own fluids. This means they exert less osmotic pressure than ECF, which allows water to move into the cell or ICF compartment. Hypotonic solutions are often used to treat intracellular fluid volume deficit conditions, such as diabetic ketoacidosis or hyperosmolar hyperglycemic state (Epstein & Waseem, 2022).

Hypertonic Solutions

Hypertonic solutions have a higher concentration of dissolved particles than the body's own fluid, which means

they exert greater osmotic pressure than ECF. This results in a higher solute concentration than the serum, thus pulling water from the interstitial space into the ECF and causing cell shrinkage. They are used to treat conditions such as severe hyponatremia (low sodium levels), cerebral edema (swelling of the brain), or increased intracranial pressure (ICP) (Epstein & Waseem, 2022).

Colloid Solutions

Colloid solutions, also known as *volume expanders*, differ from crystalloid solutions in that they contain large molecular structures, such as proteins, carbohydrates, and lipids, that increase their osmolality without dissolving in the solution. Due to their large size, colloid solutions cannot cross the semipermeable membrane of capillary walls and remain confined to the intravascular compartment. These solutions increase the colloidal oncotic pressure, which draws fluid from the interstitial space into plasma, resulting in an increase in blood volume.

Commonly administered colloidal solutions are listed in Table 5.1 along with their indications and precautions (Crosignani et al., 2022).

Crystalloid Intravenous Solutions			
Solution Classification	**Common Fluid Names**	**Indications**	**Precautions**
Isotonic	Lactated Ringer's (LR) 0.9% normal saline (NaCl) 5% dextrose in water (D_5W)	• Rehydration and sodium repletion • Dextrose supplies calories	• May cause fluid volume excess in clients with heart and renal disorders • Do not administer to clients with increased intracranial pressure
Hypotonic	0.45% normal saline (1/2 NaCl) 0.33% normal saline (1/3 NaCl)	• Replaces intracellular fluid volume deficit • Provides free water to allow excretion of body wastes	• Do not administer to clients with increased ICP
Hypertonic	3% normal saline (3% NaCl) 10% dextrose in water ($D_{10}W$)	• Increases serum osmolality • Corrects severe hyponatremia • Decreases intracranial pressure (ICP)	• May cause hypervolemia and pulmonary edema • High concentrations of dextrose must be administered through a central venous catheter (do not administer through a peripheral intravenous catheter because this may cause vein irritation/damage or thrombosis) • Administer via IV infusion device/pump and monitor electrolytes closely
Colloidal Intravenous Solutions			

TABLE 5.1 **Fluid Replacement: Crystalloid and Colloid Intravenous Solutions** (sources: FADIC, n.d.; Rudloff & Hopper, 2021; Tinawi, 2021)

Solution Classification	Fluid Names	Indications	Precautions
High molecular weight	Dextran 75 Dextran 70 6% in 5% dextrose	• Repletion of fluid volume	• Monitor closely for signs of fluid volume excess during therapy • May interfere with laboratory testing (diluting hemoglobin and hematocrit) and blood typing and cross match—draw blood before administering IV solution • Contraindicated in clients with heart, kidney, liver, or bleeding disorders
Hydroxyethyl starch	Hetastarch 6% Hespan Hextend	• Repletion of fluid volume	• Monitor closely for signs of circulatory overload such as shortness of breath, high blood pressure, and swelling in legs, ankles, or feet during therapy • Interferes with platelet function by increasing bleeding time • Contraindicated in clients with bleeding disorders or cardiac, kidney, or liver disorders
Human albumin	Albumin 5% Albumin 25%	• Albumin 5% is more commonly used in the treatment of volume loss such as in dehydration • Albumin 25% is the therapeutic choice when either sodium or fluid is restricted or in colloidal osmotic pressure deficiencies	• Monitor closely for signs of fluid volume excess during therapy • Contraindicated in clients with heart failure or severe anemia • Hold (do not administer) ACE inhibitors 24 hours before administering albumin due to risk of adverse reactions such as flushing and hypotension (Kumar et al., 2020)

TABLE 5.1 **Fluid Replacement: Crystalloid and Colloid Intravenous Solutions** (sources: FADIC, n.d.; Rudloff & Hopper, 2021; Tinawi, 2021)

SAFETY ALERT

Hydroxyethyl Starch (HES) Product Risk

Use of hydroxyethyl starch (HES) products increases the risk of mortality, kidney injury, and coagulopathy. Do not use HES products (such as hetastarch) unless an adequate alternative treatment is unavailable.

Total Parenteral Nutrition

Total parenteral nutrition (TPN), also known as *intravenous nutrition*, is a medical treatment that involves administering a specialized nutritional formula directly into a person's bloodstream through a central venous catheter. The nutritional formula is tailored to the specific needs of the client and typically includes amino acids, carbohydrates, proteins, fats, electrolytes, vitamins, and minerals (Hamdan & Puckett, 2022).

TPN is used for clients who are unable to receive adequate nutrition through their digestive system due to illness, injury, or surgery. TPN is administered through a central venous catheter (central line, peripherally inserted central catheter, or an implanted port), which is placed in a large vein that terminates in the superior vena cava. The administration rate and duration of TPN depends on the client's condition and response to treatment (Hamdan & Puckett, 2022).

SAFETY ALERT

TPN and Peripherally Inserted Venous Catheters

Due to its high osmolality, TPN should not be administered through a peripheral venous catheter because it can cause vein irritation, damage, or thrombus formation (American Society for Parenteral and Enteral Nutrition, n.d.).

Indications for TPN include:

- Severe malnutrition
- Gastrointestinal disorders that prevent the absorption of nutrients
- Severe burns
- Inflammatory bowel disorders or diseases
- Short bowel syndrome
- Cancer or cancer treatments that affect the digestive system

Contraindications for TPN include:

- Intestinal obstruction or perforation
- Hepatic impairment
- Kidney impairment
- Uncontrolled diabetes

Adverse Effects

Adverse effects for TPN include:

- Catheter site infection
- Fluid volume overload
- Hyperglycemia
- Hypoglycemia if discontinued suddenly
- Parenteral-associated cholestasis
- Bleeding
- Refeeding syndrome
- Venous thrombosis

Clients should be monitored closely until they are stable. Monitoring should include (Hamdan & Puckett, 2022):

- Intake and output every 12 hours
- Urine sugar monitoring every 8 hours
- Serum electrolyte levels
- Serum protein levels
- Liver function levels

Blood and Blood Products

As you may recall, blood is a complex bodily fluid that is essential for transporting oxygen, nutrients, and hormones to the body's tissues and organs as well as removing waste products. Blood products are components of blood that have been separated from whole blood through a process called **blood fractionation**. This process involves dividing the blood into red blood cells, platelets, and plasma and then processing and storing them separately (American Red Cross, n.d.).

Packed Red Blood Cells (PRBCs)

Packed red blood cells (PRBCs) are a blood product that contains concentrated red blood cells. PRBCs are created by removing most of the plasma from donated blood, leaving behind a concentrated mixture of red blood cells. PRBCs are used to treat conditions such as anemia, blood loss, or other conditions that require a boost in red blood cells. PRBCs are typically stored in a refrigerator unit in a blood bank and have a shelf life of up to 42 days (American Red Cross, n.d.).

Platelets

Platelets are another type of blood cell that plays a crucial role in blood clotting. They help to plug damaged blood vessels and prevent excessive bleeding. Platelets can be separated from donated blood and are used to treat conditions such as thrombocytopenia, which is a low platelet count (American Red Cross, n.d.).

Fat Emulsions (Lipids)

Fat emulsions, also known as *lipids*, are a substance found in the bloodstream. They include cholesterol, triglycerides, and other types of fatty acids. Lipids are given to clients who have a deficiency of fatty acids. Lipids are commonly administered along with TPN via piggyback or combined into the total TPN formula (Ahmed et al., 2023; American Red Cross, n.d.; Sepulveda & Pak, 2022).

Cryoprecipitated Anti-hemophilic Factor (Cryo)

Cryoprecipitated anti-hemophilic factor (cryo) is a blood product that contains a concentrated mixture of proteins used to treat bleeding disorders such as hemophilia. It is produced by freezing and thawing a unit of plasma and then removing the resulting precipitate. Cryo contains factors such as **fibrinogen**, **von Willebrand factor**, and **Factor VIII**, which are essential for blood clotting (American Red Cross, n.d.; Sachais & Senaldi, 2019).

Blood Typing, Cross-Matching, and Transfusion

Blood and blood products must be compatible with the recipient's blood type to minimize the risk of transfusion reactions. Blood typing involves determining the blood group and Rh factor of the donor and the recipient. There are four main blood groups: A, B, AB, and O. Each group can be either Rh positive or Rh negative. The donor blood type is determined by testing for the presence of specific antigens on the surface of red blood cells (American Red Cross, n.d.).

Cross-matching involves mixing a sample of the donor's blood with a sample of the recipient's blood to check for compatibility. This is done to identify any potential reaction between the donor and recipient's blood, such as the development of antibodies or **agglutination** (clumping) of the red blood cells (Harris & Crookston, 2022).

Once the blood has been typed and cross-matched, it can be transfused into the recipient's bloodstream. An adult client will need a 16–18 gauge IV catheter for rapid transfusions and a 20–22 gauge IV catheter for routine transfusions. A pediatric client will need a 22–25 gauge IV catheter for transfusions. The length of the blood transfusion depends on the amount of blood or blood product being transfused and the rate of infusion. Generally, a unit of PRBCs takes about 2–4 hours to transfuse; other blood products such as platelets may take less time (Lotterman & Sharma, 2022).

During the transfusion, the client's vital signs should be monitored regularly and per the facility's protocol. The client should be observed closely for any signs of a transfusion reaction, which can range from mild to severe. Common reactions to blood transfusions include (Harris & Crookston, 2022; Lotterman & Sharma, 2022):

- *Febrile reactions:* the most common type of transfusion reaction, characterized by a fever and chills
- *Allergic reactions:* can range from mild itching, hives, and shortness of breath to severe anaphylaxis, which can be life-threatening
- *Hemolytic reactions:* occur when the body's immune system attacks the transfused blood cells, causing them to break down
- *Transfusion-associated circulatory overload:* occurs when the body cannot handle the volume of fluid being transfused, leading to fluid volume excess and/or heart failure

It is important to note that blood transfusions are generally safe and effective when administered properly. Health care providers can take steps to minimize the risk of transfusion reactions, including premedicating with acetaminophen and diphenhydramine. Clients are closely monitored during and after the transfusion to ensure their safety.

Correcting Fluid Imbalance

Fluid imbalance in the body can be corrected by addressing the underlying cause of the imbalance. The goal is to restore the fluid balance through various interventions. The two main types of fluid imbalances are fluid volume deficit and fluid volume excess. Correcting fluid imbalances is critical to promoting normal physiological function.

Correcting Fluid Volume Deficit

As you may recall, fluid volume deficit occurs when the body loses more fluid than it takes in. Correction of fluid volume deficit includes oral rehydration with electrolyte solutions and water and treating the underlying cause, such as vomiting, diarrhea, or excessive sweating. IV fluid therapy may need to be administered by a health care professional after a thorough physical examination and review of laboratory values (Melendez-Rivera & Anjum, 2022). Fluid volume deficit is commonly treated with a crystalloid solution (see Table 5.1); however, it may occasionally require a colloid volume expander and/or blood or blood products to prevent further fluid loss and promote recovery.

Correcting Fluid Volume Excess

Fluid volume excess occurs when the body retains more fluid than it excretes. Correcting fluid volume excess involves restricting fluid and sodium intake, using diuretics to increase urine output, and treating the underlying causes, such as heart failure or kidney disorders, to prevent further accumulation of fluid and to promote healing (Ekinci et al., 2018).

5.4 Vitamins, Minerals, and Complementary and Alternative Therapies

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 5.4.1 Discuss water-soluble and fat-soluble vitamins and their importance in the body.
- 5.4.2 Identify minerals to treat deficiencies.
- 5.4.3 Discuss chelating agents to remove excess copper, iron, and lead from the body.
- 5.4.4 Identify food source and deficiency conditions associated with vitamins and minerals.
- 5.4.5 Describe the use of common complementary and alternative therapies.
- 5.4.6 Explain how complementary and alternative therapies may potentiate, negate, or cause toxicity with prescribed drugs.
- 5.4.7 Discuss the nursing implications related to complementary and alternative therapies.
- 5.4.8 Explain the client education related to complementary and alternative therapies.

Vitamins and **minerals** are essential nutrients that the body requires for various physiological functions, including growth, development, and maintenance. Complementary and alternative therapies such as acupuncture, aromatherapy, and herbal supplements are becoming increasingly popular as nontraditional treatments for various medical conditions. This section of the chapter will discuss vitamins, minerals, and common complementary and alternative therapies.

Vitamins

Vitamins are essential organic compounds required for normal metabolic function, growth, and healing. The body requires only small amounts of vitamins daily, which are typically obtained through a well-balanced diet. Vitamins are usually prescribed for clients who have the inability to metabolize and absorb vitamins, such as with celiac disease; increased vitamin losses, such as with diarrhea and crash diets; and when there is an increased vitamin need, such as with pregnancy. There are two types of vitamins, water-soluble and fat-soluble, discussed in the following sections.

Water-Soluble

Water-soluble vitamins dissolve in water. They are excreted by the kidneys in urine and are minimally stored in the body. Water-soluble vitamins need to be consumed regularly in the diet or through supplements to maintain adequate levels in the body. They play a critical role in various bodily functions, such as energy, metabolism, nerve function, and collagen synthesis. Water-soluble vitamins, their functions, food sources, and deficiency conditions are also discussed in Table 5.2.

Fat-Soluble

Fat-soluble vitamins dissolve in fat and are stored in the body's fat tissues and liver. They are absorbed along with dietary fat and can be stored in the body for extended periods. Excessive intake of fat-soluble vitamins can lead to toxicity because they are not readily excreted. Fat-soluble vitamins are essential to various bodily functions such as vision, immune function, blood clotting, and bone health. Fat-soluble vitamins, their functions, food sources, and deficiency conditions are also discussed in Table 5.2.

Water-Soluble Vitamins			
Vitamin	**Function**	**Food Source**	**Deficit Conditions**
B_1 (Thiamine)	Promotes carbohydrate metabolism and nerve function	Whole-grain and enriched breads and cereals, nuts, liver, black beans, and meats such as fish (richest source), liver, and pork	Metabolic disorders, wet and dry beriberi, Wernicke's encephalopathy, and Korsakoff's psychosis
B_2 (Riboflavin)	Promotes use of carbohydrates, fats, and proteins necessary for red blood cell function; biggest role is with protein to promote wound healing	Whole grains, enriched grains, organ meats, and dairy products	Angular stomatitis, cheilosis, glossitis, itchy dermatitis of scrotum or vulva, microcytic anemia, and alcohol substance use disorders
B_3 (Niacin)	Essential for metabolism, glycogenolysis, and nerve function; participates in the synthesis of steroid hormones and fatty acids	Fish, poultry, peanuts, mushrooms, and whole grains	Pellagra, hepatotoxicity, and anorexia
B_9 (Folic acid)	Necessary for DNA and **heme synthesis** and intestinal functioning	Leafy vegetables such as spinach and broccoli, yellow vegetables such as squash, liver, dried beans, and peas	Megaloblastic anemias, intestinal disturbances, fetal neural tube defects (caused by deficiency during pregnancy)
B_{12} (Cobalamin)	Synthesis and maintenance of **myelin**; involved in protein synthesis and an essential factor in the synthesis of DNA; helps form red blood cells and assist in nerve function	Fish, poultry, liver, eggs, and dairy products	Poor growth, interruption or delay of nerve impulse transmission, and pernicious anemia
C (Ascorbic acid)	Essential for tissue repair and wound healing, necessary for formation of collagen; facilitates absorption of iron	Citrus fruits and juices, strawberries, kiwi, potatoes, tomatoes, and cantaloupe	Poor wound healing, bleeding gums, and scurvy
Fat-Soluble Vitamins			
Vitamin	**Function**	**Food Source**	**Deficit Conditions**
A (Retinol and beta carotene)	Necessary for immune function and healthy eyes, skin, and hair	Carrots, potatoes, pumpkins, spinach, beef, and eggs	Night blindness, skin lesions, xerophthalmia, and brittle hair
D3 (Cholecalciferol) D2 (Ergocalciferol)	Facilitates equilibrium of phosphorus and calcium, crucial for maintaining strong teeth and bones	Milk and other dairy products, such as yogurt and cheese	Rickets, osteomalacia, and osteoporosis

TABLE 5.2 **Common Water-Soluble and Fat-Soluble Vitamins** (sources: Lykstad & Sharma, 2023; Reddy & Jialal, 2022)

E (Alpha-tocopherol)	Promotes functioning of red blood cells, muscles, and tissues and is essential in anti-inflammatory processes, platelet aggregation, and immune response	Fortified cereals, whole grain products, vegetable oils, wheat germ, seeds, and nuts	Retinopathy, peripheral neuropathy, and ataxia
K (Phytonadione)	Necessary for blood clotting	Dark green leafy vegetables, turnips, and beets	Increased clotting time, bleeding, or hemorrhage

TABLE 5.2 Common Water-Soluble and Fat-Soluble Vitamins (sources: Lykstad & Sharma, 2023; Reddy & Jialal, 2022)

Minerals

Minerals are inorganic substances that are essential for certain physiological functions. Minerals are necessary for the formation of strong bones and teeth, regulation of fluid balance, muscle function, and the production of hormones and enzymes. They aid in the transport of oxygen and nutrients throughout the body and support immune function. Table 5.3 lists the heavy metal minerals iron, copper, lead, and zinc and their functions, food sources, chelating agents for toxicity, and deficiency conditions. Table 5.4 lists the functions, food sources, and deficiency conditions for zinc, chromium, and selenium.

Mineral	Function	Food Source	Chelating Agents for Toxicity	Deficiency Conditions
Iron	Component of hemoglobin, helps transport oxygen, supports immune function, and assists in the production of energy	Red meat, poultry, fish, beans, lentils, tofu, fortified cereals, spinach, and other leafy greens	Deferoxamine, deferasirox, and deferiprone bind to excess iron in the body, forming a complex that can then be excreted in the urine or feces. They are used to treat iron overload conditions such as hemochromatosis or thalassemia.	Iron deficiency anemia (microcytic, hypochromic), pregnancy (due to an increased need for RBCs as a result of increased blood volume and the fetus), gastrointestinal bleeding
Copper	Helps form red blood cells, supports immune function, and assists in the production of energy and collagen; required for melanin production	Shellfish, nuts, seeds, whole grains, beans, and dark leafy greens	Penicillamine and trientine bind to excess copper and form a complex that can be excreted in the urine. They are used to treat Wilson's disease, a genetic disorder that causes copper to accumulate in the liver and brain.	Celiac disease, excessive zinc intake (which can interfere with copper absorption and utilization), and Menkes' disease (a hereditary abnormality that blocks absorption of copper)
Lead	Is a toxic heavy metal and has no known essential functions within the body but through exposure can lead to a variety of health problems	Found in contaminated water and food supplies, especially in areas of high environmental pollution and in older homes with lead-based paint or pipes	Dimercaprol, EDTA, and succimer bind to lead in the body, forming a compound that is excreted in the urine or feces; they are used to treat lead poisoning and reduce the body burden of lead.	No deficiency conditions

TABLE 5.3 **Heavy Metal Minerals and Chelating Agents** (sources: Fisher & Gupta, 2022; Moses, 2021; Rajkumar et al., 2023)

Mineral	Function	Food Source	Deficiency Conditions
Zinc	Supports immune function, helps with wound healing, assists in the production of proteins and DNA synthesis, involved in taste acuity	Oysters, beef, pork, chicken, beans, nuts, seeds, and whole grains	Crohn's disease, celiac disease, pregnancy, growth retardation, delayed sexual maturation, alopecia, loss of taste sensation, poor wound healing, impaired immunity
Chromium	Helps regulate blood sugar levels by potentiating the action of insulin; supports healthy metabolism	Broccoli, grape juice, whole grains, and nuts	Chromium deficiency is rare because the body requires only small amounts; however, severe deficiencies can cause glucose intolerance and weight loss.
Selenium	Acts as an antioxidant and helps protect cells from damage, supports immune function, necessary for iodine metabolism to assist in the production of thyroid hormones	Brazil nuts, seafood, poultry, beef, eggs, and whole grains	Malabsorption syndrome

TABLE 5.4 **Common Minerals** (sources: Fisher & Gupta, 2022; Moses, 2021)

Complementary and Alternative Therapies

Complementary and alternative therapies, also known as *complementary and alternative medicine (CAM)*, is a broad term used to describe health practices and treatments that are used in addition to or instead of conventional medical therapies. Examples of CAM include herbal supplements, acupuncture, chiropractic care, massage therapy, and mind-body practices such as meditation and yoga. Some people choose CAM therapies because they believe they are more natural or holistic than conventional medicine or because they have had negative experiences with conventional medicine (Jones et al., 2019; National Institutes of Health, n.d.-b). However, it is important to note that not all CAM therapies are safe and effective, and some may even be harmful.

Dietary Supplement and Health Education Act

The Dietary Supplement and Health Education Act (DSHEA) of 1994 is a federal law that regulates the manufacturing and labeling of dietary supplements. Under DSHEA, dietary supplements are classified as a food, not a drug, and are not subject to the same strict regulations as drugs. However, DSHEA does require that manufacturers of dietary supplements meet certain labeling requirements and notify the Food and Drug Administration (FDA) of any new ingredients they plan to use. DSHEA also allows manufacturers to make certain health claims about their products as long as they are truthful and not misleading (National Institutes of Health, n.d.-a).

Good Manufacturing Practices

Good Manufacturing Practices (GMPs) are a set of guidelines established by the FDA that ensures quality, purity, and strength of dietary supplements. GMPs require manufacturers to use standardized manufacturing processes, perform regular testing of raw materials and finished products, and maintain detailed records of all production and testing. GMPs also require manufacturers to have a system in place for handling complaints and reporting adverse events (National Institutes of Health, n.d.-a).

Commonly Used Herbal Remedies

There are numerous herbal remedies that are used by the general public. Table 5.5 presents common herbal

remedies, their use, and special considerations.

Herbal Remedy	Use	Special Considerations
Astragalus	To increase stamina and energy and to improve immune function	May increase effects of anti-hypertensive drugs (Han et al., 2019); caution should be used when administering if the client has a fever because it can mask infection
Chamomile	Used topically to treat wounds and conjunctivitis; used orally for migraines and anxiety	Clients should not take if pregnant or breastfeeding because it can harm the fetus/infant, can interact with anticoagulants and increase bleeding times, and may cause depression
Echinacea	To enhance the immune system and treat colds and influenza; suppresses inflammation	Usage for longer than 12 weeks may cause liver toxicity; do not use with antifungals or hepatotoxic drugs; usage in immunocompromised clients is discouraged
Garlic	To treat colds; for cardiovascular health (reduces levels of triglycerides and LDL and raises levels of HDL); helps to reduce blood pressure and suppress platelet aggregation and lower blood glucose levels	Has anticoagulant effects and should be used cautiously in clients on anticoagulants; lowers blood glucose levels and may cause hypoglycemia in clients already taking medications for their diabetes; reduces triglycerides and LDL and increases HDL levels—may need a dosage adjustment if client is taking medications for lipids
Ginger	To treat nausea, motion sickness, and postoperative nausea; also has anti-inflammatory and analgesic properties	Affects blood clotting and is contraindicated for clients on anticoagulants
Ginseng	To treat hypertension; also is a mood elevator and decreases cholesterol levels	May cause irritability if taken with caffeine; may cause interactions with phenelzine and monoamine oxidase inhibitors (MAOIs); may interfere with the effectiveness of digoxin
Hawthorn	To treat blood pressure problems and lower cholesterol levels	Use cautiously with digoxin, ACE inhibitors, and central nervous system (CNS) depressants because it may potentiate their effects

TABLE 5.5 **Common Herbal Remedies: Uses and Special Considerations** (source: Furhad & Bokhari, 2022; National Institutes of Health, n.d.-c.)

Herbal Remedy	Use	Special Considerations
Licorice root	To treat cough and stomach ulcers	Contraindicated with renal or liver disease, hypertension, coronary artery disease, and pregnancy and in clients who are taking digoxin and thyroid drugs
Milk thistle	To treat fatty liver and hepatitis	Can potentiate antihypertensive drugs and immunosuppressant drugs
Saw palmetto	To treat urinary symptoms related to prostate issues	May cause orthostatic hypotension; do not use with finasteride because toxicity may occur (Mount Sinai, n.d.)
St. John's wort	To treat depression	Take on an empty stomach to enhance absorption; may interact with other antidepressants as well as theophylline, digoxin, hormonal contraceptives, and certain anticancer drugs; client should not take if pregnant or breastfeeding because it may affect the fetus/infant
Turmeric	To treat inflammation	May cause gastrointestinal upset and may increase bleeding times if used with oral anticoagulants
Valerian	To treat insomnia and anxiety	May cause severe liver damage; should not be used with CNS depressants because it may cause severe sedation

TABLE 5.5 **Common Herbal Remedies: Uses and Special Considerations** (source: Furhad & Bokhari, 2022; National Institutes of Health, n.d.-c.)

Common Complementary Therapies

Complementary therapies are used to promote overall health and well-being. They are often used to alleviate symptoms and side effects associated with medical conditions and treatments, but they are not intended to replace or serve as a substitute for traditional medical care. Table 5.6 describes common complementary therapies, their uses, and special considerations.

SPECIAL CONSIDERATIONS

Asian Americans and CAM

Asian Americans are more likely to use complementary and alternative medicine (CAM) as compared to other races or ethnicities. Many continue cultural traditions of using Eastern alternatives such as acupuncture, Ayurveda, and yoga.

(Source: Felicilda-Reynaldo et al., 2020.)

TRENDING TODAY

Cannabis and Health Care

Access multimedia content (https://openstax.org/books/pharmacology/pages/5-4-vitamins-minerals-and-

complementary-and-alternative-therapies)

Cannabis has been used for centuries as a natural remedy to alleviate symptoms of various health conditions, such as chronic pain, anxiety, and insomnia. Medical cannabis is a new trend that is legal in many states and countries, allowing clients access to cannabis-based treatments under the supervision of licensed health care providers. With the increasing use of medical cannabis, there is a growing need for health care professionals to be trained in its use and to be able to provide accurate information to clients. Dr. Josh Axe, DNM, DC, CNS, is a doctor of natural medicine, chiropractor, and clinical nutritionist. In the video podcast "Medicinal Benefits of Cannabis Compounds," Dr. Axe interviews Dr. Bonni Goldstein, MD, who speaks about the different types of cannabis and its medicinal benefits.

Complementary Therapy	Definition	Use	Special Considerations
Acupuncture	A traditional Chinese medical practice that involves inserting thin needles into specific points on the body to promote healing and pain relief	Treatment of chronic pain, headaches, and musculoskeletal problems	Risk for infection and injury from the needles; not appropriate for people who are taking immunosuppressant or anticoagulant drugs; contraindicated in clients who have diabetes, stroke, or other neurological conditions
Aromatherapy	The use of essential oils to promote physical and emotional well-being	Stress reduction, improvement of mood, and promoting relaxation	May cause skin irritation or an allergic reaction
Ayurveda	A traditional Indian medical practice that seeks to balance the body, mind, and spirit through diet, lifestyle changes, and herbal remedies	Treatment of digestive disorders, anxiety, and skin problems	Herbal remedies may interact with prescription drugs and should not be used without speaking to the health care provider; some products may contain heavy metals or other toxins
Cannabis (marijuana)	A plant that contains compounds that have psychoactive effects	Treatment of chronic pain, muscle spasms, seizures, and nausea and vomiting associated with chemotherapy, and to increase appetite	May cause impaired coordination and memory, increased heart rate, and temporary cognitive impairment; may be addictive
Touch therapy	A form of healing that involves the use of touch to promote relaxation and reduce stress	Treatment of anxiety, depression, and chronic pain	Contraindicated in skin conditions where touch therapy may exacerbate the condition, areas of recent injuries or surgery, or areas where cancer treatment such as radiation therapy is being administered

TABLE 5.6 **Common Complementary Therapies** (sources: Kisling & Stiegmann, 2022; National Institutes of Health, n.d.-a)

Chapter Summary

This chapter has provided an overview of various aspects of well-being including fluid balance, electrolytes, vitamins, minerals, and complementary and alternative therapies. The body relies on precise fluid balance to maintain healthy physiologic functions. Disruptions to this balance can lead to health complications and even death. Electrolytes, such as sodium, calcium, and potassium, play a crucial role in maintaining fluid balance. In addition, they have a major effect on neurotransmission and muscular contraction. Changes in nerve and muscle excitability can be life-threatening. Vitamins and minerals are essential nutrients that the body requires in small amounts. Their deficiencies or excesses can result in a range of health issues. Additionally, complementary and alternative therapies, such as acupuncture and herbal remedies, are becoming increasingly popular as a means of promoting health and well-being. Understanding these various components of wellness is important for health promotion and disease prevention.

Key Terms

agglutination the clumping of particles
blood fractionation the process of separating blood into its component parts
blood products substances derived from human blood
colloid solutions a solute in a solution of molecules or ions
colloidal oncotic pressure osmotic pressure that causes fluid to pull back into the capillary by large molecules such as proteins
complementary and alternative therapies medical products and practices outside of conventional medical practice; complementary therapies are used as adjuncts to conventional therapies, and alternative therapies are used in place of conventional therapies
cryoprecipitated anti-hemophilic factor (cryo) a portion of plasma that is rich in clotting factors
crystalloid solutions a solute in a solution that lacks proteins and insoluble molecules
electrolytes essential minerals that carry an electric charge and are crucial for functions like nerve signaling, muscle contraction, and fluid balance in the body
extracellular fluid (ECF) fluid outside of the cell
Factor VIII a blood clotting factor that when deficient causes bleeding
fat emulsions a liquid composed of fat and water
fat-soluble vitamins vitamins that dissolve in fat; includes vitamins A, D, E, and K
fibrinogen a protein that assists with forming blood clots
fluid volume the volume of intracellular and extracellular fluids in the body
fluid volume deficit a condition where fluid output exceeds fluid intake
fluid volume excess a condition where the body retains more fluid than it excretes
glycolysis the process of converting glucose into pyruvate, an important metabolic product for energy
heme synthesis a biochemical pathway that requires a number of steps, substrates, and enzymes
hypertonic solutions a solution with a high solute concentration and a low water concentration
hypervolemia the condition of fluid volume excess
hypotonic solutions a solution with a low solute concentration and a high water concentration
hypovolemia the condition of fluid volume deficit
intracellular fluid (ICF) fluid inside the cell
intravenous (IV) fluid therapy the process of administering fluids through a vein
isotonic solutions a solution that has the same solute and water concentrations as the cytoplasm of the cell
minerals inorganic substances that are essential for certain physiological functions
myelin a mixture of proteins and phospholipids that form an insulating sheath around nerve fibers
packed red blood cells (PRBCs) a blood product that contains concentrated red blood cells
platelets cells that are responsible for clotting blood
shock a condition caused by a sudden decrease in blood flow
sodium-potassium-ATPase pump (Na^+K^+ATPase pump) responsible for the transport of sodium ions out of cells and potassium ions into cells against their concentration gradients
total parenteral nutrition (TPN) intravenous nutrition
vitamins essential organic compounds required for normal physiological function
von Willebrand factor a blood disorder that prevents the blood from clotting
water-soluble vitamins vitamins that dissolve in water; includes vitamins B and C

Review Questions

1. A nurse is to administer 1 L of 5% dextrose in water (D_5W) over 6 hours. The IV set delivers 10 drops per milliliter. What is the drip rate per minute that the nurse should set? Round to the nearest whole number.
   a. 27 drops per minute
   b. 28 drops per minute
   c. 29 drops per minute
   d. 30 drops per minute

2. Which of the following is a water-soluble vitamin that is important for the synthesis of collagen and wound healing?
   a. Vitamin A
   b. Vitamin E
   c. Vitamin C
   d. Vitamin K

3. The nurse is caring for a client with fluid volume excess. Which of the following interventions would be appropriate for this client?
   a. Encourage fluid intake
   b. Administer diuretic drugs
   c. Increase dietary sodium intake
   d. Administer intravenous replacement fluids

4. The nurse is caring for a client who is receiving a blood transfusion. During the transfusion, the client develops itching, hives, and shortness of breath. The nurse recognizes that these symptoms are most likely indicative of which of the following?
   a. Hemolytic reaction
   b. Febrile reaction
   c. Allergic reaction
   d. Circulatory overload

5. The health care provider orders 750 mL of lactated Ringer's solution to be administered over 8 hours. What is the appropriate rate in milliliters per hour to set the IV infusion pump? Round to the nearest whole number.
   a. 94
   b. 93
   c. 92
   d. 91

6. Which of the following is a fat-soluble vitamin that can accumulate in the body and potentially cause toxicity?
   a. Vitamin B_6
   b. Vitamin B_{12}
   c. Vitamin C
   d. Vitamin A

7. The nurse is caring for a client with fluid volume deficit. Which of the following findings would the nurse expect to assess in this client?
   a. Edema
   b. Tachycardia
   c. Elevated blood pressure
   d. Crackles in the lungs

8. The nurse is caring for a client who has been prescribed calcium supplements for the treatment of osteoporosis. Which of the following should the nurse instruct the client to take 1 hour before or after the administration of calcium supplements?

a. Vitamin D
b. Zinc
c. Magnesium
d. Iron

9. A nurse is caring for a client who has been taking echinacea for the treatment of a cold. Which of the following should the nurse monitor the client for while they are taking echinacea?
a. Coagulation
b. Liver function
c. Renal function
d. Cholesterol

10. The nurse is caring for a client who has been taking St. John's wort for the management of depression. Which of the following should the nurse instruct the client about regarding the use of St. John's wort?
a. It may cause weight gain and fluid retention.
b. It is safe to use during pregnancy.
c. It should be taken with food.
d. It may interact with other drugs such as antidepressants.

CHAPTER 6

Introduction to the Immune System and the Inflammatory Response

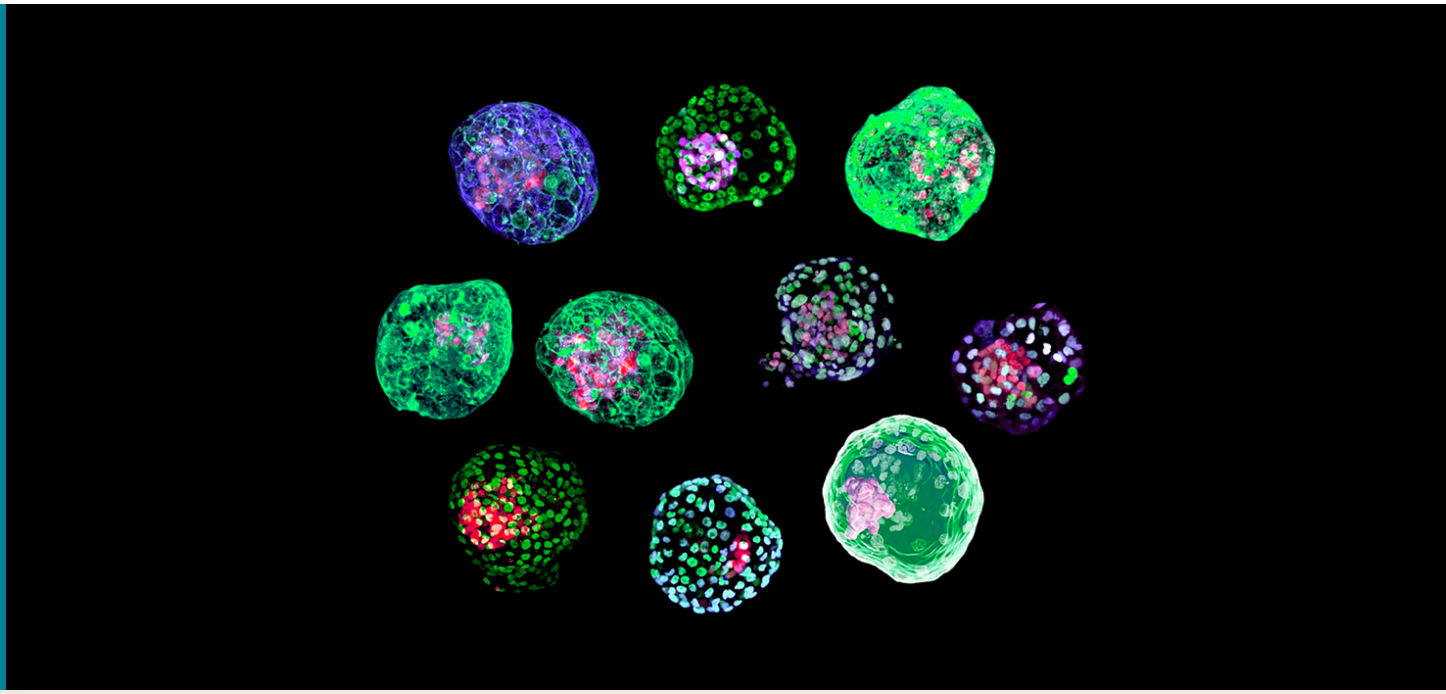


FIGURE 6.1 The immune system is a complex network of cells, tissues, and organs that work together to protect the body from harmful substances, such as pathogens. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The **immune system** is an intricate defense mechanism that protects the human body from diseases and infection. It uses antibodies and white blood cells to combat foreign invaders such as bacteria and viruses. Maintaining a healthy immune system is essential for overall well-being and resilience against potential harm. This section of the chapter will discuss the immune system and its function, explain antigen-antibody interactions, and compare antibody-mediated and cell-mediated immunity.

6.1 Introduction to Immunity

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 6.1.1 Discuss the immune system and its function.
- 6.1.2 Compare and contrast antibody-mediated immunity and cell-mediated immunity.
- 6.1.3 Explain antigen-antibody interactions.

The Immune System

The immune system is a complex and sophisticated defense mechanism that protects the human body from harmful pathogens, such as bacteria, viruses, and other foreign substances (Justiz-Vaillant et al., 2022). It is composed of

various cells, tissues, and organs. These components work in harmony to identify, neutralize, and eliminate foreign invaders by distinguishing between self and non-self and recognizing specific patterns found on the surface of a pathogen.

There are two main branches of the immune system: the **innate immune system** and the **adaptive immune system** (as seen in Figure 6.2). The innate immune system provides the first line of defense and is always "on." It acts rapidly upon encountering pathogens (Justiz-Vaillant et al., 2022). It includes physical barriers like the skin, hair, and mucous membranes as well as certain white blood cells, such as basophils, mast cells, monocytes, neutrophils, and macrophages, that respond quickly to infections.

When a pathogen breaches the innate defenses, the adaptive immune system (also known as the acquired immune system) comes into play to control infection. It is more specific to pathogens, has memory, and develops over time, through either encountering a pathogen or receiving a vaccination (Justiz-Vaillant et al., 2022).

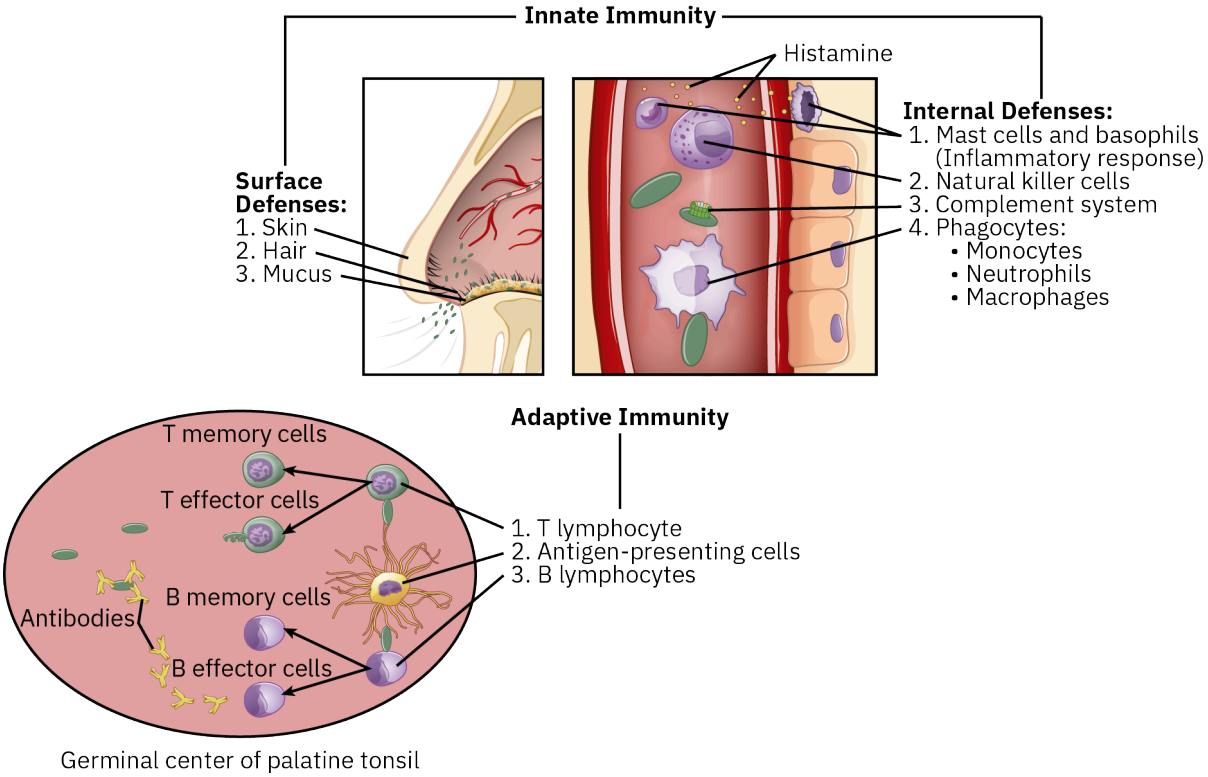


FIGURE 6.2 This image illustrates the cooperation between the innate and the adaptive immune systems in response to pathogens. The innate immune system enhances adaptive immune responses so they can be more effective. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The adaptive immune system relies on white blood cells called T and B lymphocytes. T cells produce a cell-mediated immune response, and B cells produce the humoral immune response (as seen in Figure 6.3). These immune responses will be discussed in more detail in the subsequent sections.

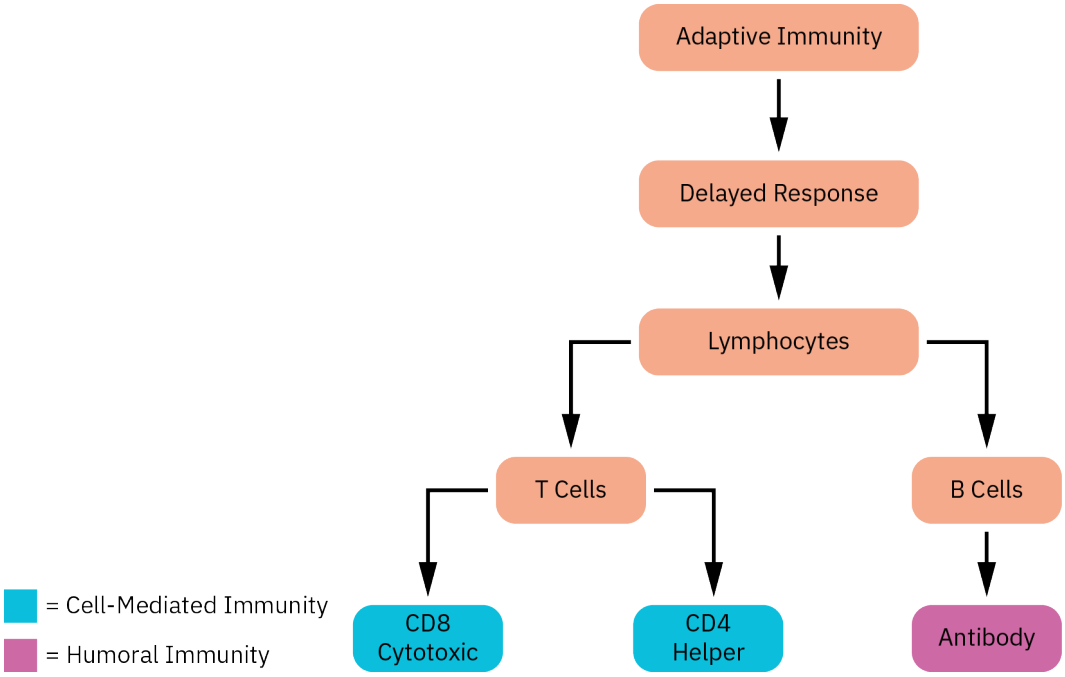


FIGURE 6.3 This diagram illustrates T cell and B cell responses. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Antibody Mediated/Humoral Immunity

Antibody mediated/humoral immunity is a type of immune response that primarily involves B cells and their production of antibodies (Karagiannis & Arnold, 2022). When an antigen, such as a pathogen, foreign substance, or vaccination, enters the body, B cells recognize it and become activated (see Figure 6.3). These activated B cells then undergo differentiation and proliferation to form plasma cells, which are specialized factories for producing antibodies. The production of antibodies increases over time, reaching peak levels within 1 to 2 weeks after the initial encounter with the antigen. During the immune response, some B cells undergo differentiation into memory B cells. These cells remain in the body even after the antigen has been cleared. Memory B cells remember the encountered antigen and can rapidly initiate a strong response if the same antigen is encountered again in the future.

Cell-Mediated Immunity

Cell-mediated immunity is an immune response that involves T cells, specifically helper T cells (CD4 cells) and cytotoxic T cells (CD8 cells). This clusters of differentiation (CD) system is a way to classify and characterize different immune cell types based on the presence of specific surface markers, and this system is particularly relevant when distinguishing subsets of T helper cells, like CD4+ and CD8+ T cells. When an antigen is presented to T cells, helper T cells become activated and play a central role in coordinating the immune response (see Figure 6.3). They release chemical signals (cytokines) that stimulate the proliferation and activation of other immune cells, including cytotoxic T cells and B cells.

Cytotoxic T cells recognize cells that display foreign antigens on their surface, such as virus-infected cells or cancer cells. Cytotoxic T cells release toxic substances that attack and kill infected or abnormal cells, effectively eliminating the cells.

Antigen-Antibody Interactions

Antigen-antibody interactions are essential for the functioning of both innate and adaptive immune responses. They help in the identification and elimination of harmful invaders as well as in the establishment of immune memory, allowing the body to mount a more rapid and efficient response upon subsequent exposure to the same antigen. This process forms the basis for vaccination, where the body is exposed to harmless versions of antigens to develop immunity without experiencing severe symptoms of the disease.

Antigen-antibody interactions are fundamental processes in the immune response that play a crucial role in

defending the body against infections and foreign substances (Karagiannis & Arnold, 2022). An antigen is a molecule or molecular structure, typically a protein or polysaccharide, that is recognized by the immune system as foreign or non-self. It can be present on the surface of pathogens such as bacteria, viruses, or parasites as well as on non-pathogenic substances like pollen or certain foods.

Antibodies, also known as immunoglobulins (Ig), are Y-shaped proteins produced by B cells in response to the presence of antigens (Aziz et al., 2023). Each antibody is specifically designed to recognize and bind to a particular antigen, much like a lock-and-key mechanism. The region of the antibody that binds to the antigen is called the antigen-binding site or paratope (Justiz-Vaillant et al., 2023; Greenspan, 2023).

When an antigen enters the body, it triggers the immune system to mount a response. B cells detect the antigen and start producing antibodies that specifically match its molecular structure. The process of antibody production and maturation takes a few days to weeks, but once antibodies are generated, they remain in the body as part of the immune memory.

The binding of antibodies to antigens is highly specific. When an antibody encounters its target antigen, it attaches to it, forming an antigen-antibody complex. This binding serves various purposes:

- Neutralization: Antibodies can neutralize pathogens or toxins by blocking their ability to infect cells or exert harmful effects.
- Opsonization: Antibodies can coat pathogens, facilitating their recognition and uptake by phagocytic cells like macrophages and neutrophils, leading to their destruction (Thau et al., 2023).
- Agglutination: Antibodies can bind to multiple antigens on the surface of pathogens, clumping them together and making it easier for phagocytes to engulf and clear them.
- Activation of complement: Antibodies can activate the complement system, a group of proteins that can lead to the destruction of pathogens through various mechanisms. Complement proteins interact like a chain reaction where one step leads to the next, creating a powerful response to invaders. This reaction is also known as a *complement cascade* (Bardhan & Kushik, 2023).

6.2 Vaccine-Preventable Diseases, Vaccines, and Immunizations

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 6.2.1 Define immunity.
- 6.2.2 Differentiate between natural and active acquired immunity.
- 6.2.3 Describe the difference between active and passive immunity.
- 6.2.4 Explain the importance of vaccination in the immunity process.
- 6.2.5 Identify common diseases that can be prevented with vaccines.
- 6.2.6 Describe the difference between vaccines and immunizations.
- 6.2.7 Review vaccination recommendations based on age and travel.
- 6.2.8 Describe nursing implications related to vaccines and immunizations.
- 6.2.9 Explain the client education related to vaccines and immunizations.

Vaccine-preventable diseases are infectious illnesses caused by viruses or bacteria that can be effectively prevented using vaccines, which stimulate the immune system to develop specific immunity against these pathogens (Centers for Disease Control and Prevention [CDC], 2023a). Vaccines are biological preparations containing weakened or inactivated pathogens or their components, prompting the body to produce protective antibodies and memory cells. Immunizations involve administering vaccines to clients, providing them with the necessary immunity to ward off specific diseases, thus reducing the risk of infection and its potential severe consequences while contributing to vital public health efforts to control and eradicate these preventable diseases.

Immunity

Immunity is the ability of an organism to resist or defend against harmful pathogens such as microorganisms or toxic substances (CDC, 2023a). It is an essential defense mechanism that helps protect the body from infections and diseases. There are different types of immunity, including natural, active acquired, active, and passive immunity, which are discussed below.

Natural Immunity

Natural immunity, also known as innate immunity, is the inborn resistance to certain diseases that a client possesses without prior exposure to the causative agent. This type of immunity is non-specific, meaning it provides a general defense against a wide range of pathogens. Natural immunity is the first line of defense and includes physical barriers (e.g., skin), chemical barriers (e.g., stomach acid), and cellular responses (e.g., macrophages and natural killer cells).

Acquired Immunity

An acquired immunity is the immunity that develops after exposure to a foreign antigen. The immune system recognizes the antigen as foreign, and a specific response is generated to target and eliminate it. This type of immunity is long lasting and involves the production of memory B cells, which "remember" the encountered antigen and can mount a faster and stronger response upon subsequent exposures (Grubbs & Kahwaji, 2022). Active acquired immunity can be achieved through two main ways:

- *Naturally acquired active immunity:* This occurs when a client is exposed to a pathogen in the environment and develops immunity as a result. For example, getting infected with a virus and recovering from the infection leads to natural active acquired immunity.
- *Artificially acquired active immunity:* This type of immunity is induced through vaccination. Vaccines contain weakened or inactivated forms of pathogens or their components, which stimulate the immune system to produce a response without causing the actual disease. The immune system then develops memory cells to provide protection against future infections by the same pathogen.

Active Immunity

Active immunity, in a broad sense, refers to immunity that is generated by the body's immune system actively responding to a foreign antigen. It encompasses both natural and active acquired immunity. This type of immunity enables a rapid and potent response upon subsequent exposures to the same pathogen.

Passive Immunity

Passive immunity is the temporary protection against a specific pathogen that is conferred to a client by receiving pre-formed antibodies rather than producing them internally (Slifka & Amanna, 2018). Unlike active immunity, passive immunity does not involve the production of memory B cells, and the protection is short-lived. Passive immunity can be acquired through two main ways:

- *Natural passive immunity:* This occurs when antibodies are passed from a pregnant person to the fetus through the placenta during pregnancy or through breast milk during breastfeeding. These antibodies provide the newborn with some protection during the early stages of life until their own immune system matures.
- *Artificial passive immunity:* This type of immunity is achieved by administering pre-formed (synthetic or pooled from donors) antibodies obtained from another individual or animal. For example, in certain medical situations, such as treating some viral infections or providing immediate protection against specific diseases, purified antibodies can be given as a treatment. The protection offered by artificial passive immunity diminishes as the administered antibodies are gradually cleared from the body.

Vaccines and Immunizations

Vaccines and **immunizations** are related concepts, but they differ in their scope and application. Vaccines are biological substances designed to stimulate the immune system and generate a protective response against specific pathogens (CDC, 2023a). They can be composed of weakened or inactivated forms of the disease-causing agent (virus, bacteria, or toxin) or subunits of the pathogen. When administered, vaccines prompt the immune system to recognize the antigens present in the vaccine and produce antibodies, memory cells, and other immune responses. These immune responses prepare the body to defend against future infections by the actual pathogen.

Immunization is the process of administering vaccines to clients, aiming to establish immunity against certain diseases (CDC, 2023a). It is a preventive measure to protect clients from infections, especially those that can cause severe illness, disability, or death. Through immunizations, clients build immunity without experiencing the full-blown disease, which reduces the risk of infection and contributes to public health by controlling the spread of disease.

Vaccines employ various mechanisms of action, and there are different types including:

- *Live attenuated vaccines:* These vaccines contain weakened but live forms of the pathogen. These weakened strains can still replicate within the body but are rendered less **virulent**, so they do not cause the disease in healthy individuals. Examples of live attenuated vaccines include the measles, mumps, rubella (MMR) vaccine and the oral polio vaccine (OPV). These vaccines generally provide long-lasting immunity with a single or few doses.
- *Inactivated vaccines:* These vaccines contain killed versions of the pathogen, meaning the virus or bacteria have been rendered nonfunctional and cannot replicate. As a result, they do not cause disease in recipients. Inactivated vaccines often require multiple doses or booster shots to build and maintain immunity. Examples of inactivated vaccines include the hepatitis A vaccine and the injectable polio vaccine (IPV).
- *Subunit, recombinant, and conjugate vaccines:* These vaccines contain only specific antigens or parts of the pathogen rather than the whole microorganism. Recombinant vaccines use genetically engineered antigens to trigger an immune response. Conjugate vaccines combine a weak antigen with a strong antigen to enhance the immune response, especially in young children. Examples of subunit, recombinant, and conjugate vaccines include the hepatitis B vaccine, human papillomavirus (HPV) vaccine, and some meningococcal vaccines.
- *mRNA vaccines*: These vaccines do not contain any live or inactivated virus or bacteria. Instead, mRNA vaccines contain genetic instructions (mRNA) that instruct the cells in the body to produce a specific viral or bacterial protein. This protein then triggers an immune response, leading to the production of antibodies and memory cells. mRNA vaccines, like the Pfizer-BioNTech and Moderna COVID-19 vaccines, have shown high efficacy and can be developed more rapidly than traditional vaccines.

Not only do vaccines and immunizations protect clients, but they also play a role in **herd immunity**. Herd immunity is a state where a significant portion of a population becomes immune to a specific infectious disease through vaccination or previous exposure (McDermott, 2021). Herd immunity works as a barrier against the transmission of the disease because the pathogen has fewer susceptible individuals to infect. The threshold required for achieving herd immunity depends on the contagiousness of the disease. For highly contagious infections like measles, a large proportion (around 95%) of the population needs to be immune to prevent outbreaks. For less contagious diseases, the threshold may be lower. Therefore, herd immunity is a crucial aspect of public health strategies and vaccination campaigns.

Vaccine hesitancy is a concerning issue and refers to the delay or refusal of vaccination despite its availability (Shen & Dubey, 2019). It is driven by factors like safety concerns, distrust in vaccines or health care providers, and misinformation. Vaccine hesitancy poses a public health challenge, as it can lead to outbreaks of preventable diseases. Addressing it requires evidence-based communication, education, and building trust to promote vaccination and protect public health.

SAFETY ALERT

Vaccines and Immunizations

The CDC and FDA monitor the safety of vaccines after they are approved. If a problem is found with a vaccine, the CDC and FDA will inform health officials, health care providers, and the public through the Global Rapid Response Team (GRRT) (https://openstax.org/r/cdcgovgloba) and through public health announcements and communications.

Vaccine-Preventable Diseases

Vaccine-preventable diseases (CDC, 2023a) are illnesses that can be avoided through vaccination. Some common vaccine-preventable diseases include measles, mumps, rubella, pertussis, polio, hepatitis A and B, varicella, human papillomavirus (HPV), pneumonia, and influenza. Vaccination against these diseases is a crucial public health measure that not only protects clients but also helps to establish herd immunity, reducing the overall prevalence and transmission of these infectious agents within communities.

Vaccine Recommendations

Vaccines are an important tool to prevent the spread of infectious diseases and protect public health. The World Health Organization (WHO, 2021; CDC, 2021) recommends routine vaccination for children against several diseases

such as measles, polio, diphtheria, tetanus, pertussis (whooping cough), and hepatitis B. Vaccination is also recommended for adults against influenza, pneumococcal disease, shingles, COVID-19, and other illnesses depending on their age, health status, occupation, travel plans, and other factors.

Vaccines have guidelines on immunization schedules for different age groups and populations based on scientific evidence and expert opinion (see Table 6.1). It is important to follow these recommendations to ensure that clients receive the appropriate vaccines at the right time and in the correct doses.

Some vaccines, such as hepatitis A and B vaccines, varicella vaccine, and MMR vaccine, require titers to assess immunity levels. A **titer** is a blood test that measures the level of antibodies against the virus in the bloodstream. Checking titers after completing the vaccination or the vaccination series helps to determine if a client has developed sufficient immunity to the virus. A positive titer indicates protective antibodies are present in the body, and the client is considered immune. If the titer is negative or below the protective level, a booster dose of the vaccine may be recommended to enhance immunity. Titers are drawn at different intervals depending on the vaccine, when vaccinated, and the client's need.

Table 6.1 provides additional information on common recommended vaccines and illustrates their indications, routes, and dosing for pediatric and adult clients.

Name	Indications for Use	Recommended Routes, Dosages, and Time
H. influenza type b (Hib) vaccine (ActHIB)	Prevention of invasive disease caused by *Haemophilus influenzae* (*H. influenzae*) type b, for use in children 2 months through 5 years of age	*A 4-dose series (0.5 mL per dose) intramuscular:* A primary 3-dose series of a single dose at 2, 4, and 6 months of age. A single booster dose at 15–18 months of age.
Hepatitis A vaccine (Havrix)	Active immunization against disease caused by hepatitis A	*Children (12 months through 18 years):* Intramuscular 0.5 mL dose and a 0.5 mL booster dose administered anytime between 6 and 12 months later. *Adults (19 years and older)*: A single 1 mL intramuscular dose and a 1 mL booster dose administered anytime between 6 and 12 months later.
Hepatitis B vaccine (Recombivax HB)	Prevention of infection caused by all known subtypes of hepatitis B virus	*Children (0–19 years of age, pediatric/adolescent formulation):* 5 mcg (0.5 mL) intramuscularly, 3 doses at 0, 1, and 6 months. *Adolescents (11–15 years of age, adult formulation):* 10 mcg (1 mL) intramuscularly, 2 doses at 0 and 4–6 months. *Adults (≥20 years, adult formulation):* 10 mcg (1 mL) intramuscularly, 3 doses at 0, 1, and 6 months. *Predialysis and dialysis clients*: 40 mcg (1 mL) intramuscularly, 3 doses at 0, 1, and 6 months.

TABLE 6.1 **Common Recommended Vaccines** (sources: https://dailymed.nlm.nih.gov/dailymed/; https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html#note-mmr)

Name	Indications for Use	Recommended Routes, Dosages, and Time
Human papillomavirus (HPV) vaccine (Gardasil, Cervarix)	Females 9–45 years of age: for the prevention of cervical, vulvar, vaginal, anal, oropharyngeal, and other head and neck cancers and genital warts caused by human papillomavirus 6, 11, 16, 18, 31, 33, 45, 52, and 58 Males 9–45 years of age: For the prevention of anal, oropharyngeal, and other head and neck cancers, and genital warts caused by human papillomavirus 6, 11, 16, 18, 31, 33, 45, 52, and 58	*Children (9–14 years):* 2 doses (0.5 mL each) intramuscularly at 0 and 6–12 months or 3 doses at 0, 2, and 6 months. *Teens and adults (ages 15–45 years):* 3 doses (0.5 mL each) intramuscularly at 0, 2, and 6 months.
Influenza vaccine (Afluria, Fluzone)	Active immunization for the prevention of influenza caused by influenza A subtype viruses and type B viruses contained in the vaccine	*Children (6–35 months):* 1 or 2 doses (0.25 mL each) intramuscularly; if 2 doses, schedule at least 1 month apart. *Children (36 months–8 years of age):* 1 or 2 doses (0.50 mL each) intramuscularly; if 2 doses, schedule at least 1 month apart. Children *(9–17 years of age):* 1 dose (0.5 mL) intramuscularly. *Adults (18–64 years of age):* 1 dose (0.5 mL) intramuscularly. *Adults ≤65 years:* High-dose quadrivalent intramuscular, 1 dose (0.7 mL).
Measles, mumps, and rubella (MMR) vaccine (M-M-R-II)	Active immunization against MMR diseases	*Children: (12–15 months and 4–6 years):* 2 doses (0.5 mL each) intramuscularly (CDC, 2021).
Meningococcal group B vaccine (Bexsero)	Active immunization to prevent invasive disease caused by *Neisseria meningitidis* serogroup B	*Children (≥5 years):* 2 doses (0.5 mL each) intramuscularly at least 1 month apart.
Pneumococcal polyvarent vaccine (Pneumovax 23)	Active immunization for the prevention of pneumococcal disease caused by the 23 serotypes contained in the vaccine	*Adults and children (≥2 years):* 1 dose (0.5 mL) intramuscularly as indicated based on the client's age and clinical condition.

TABLE 6.1 **Common Recommended Vaccines** (sources: https://dailymed.nlm.nih.gov/dailymed/; https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html#note-mmr)

Name	Indications for Use	Recommended Routes, Dosages, and Time
Pneumococcal 13-variant vaccine (Prevnar 13)	Active immunization for the prevention of pneumonia and invasive disease caused by the 13 serotypes of *S. pneumoniae* contained in the vaccine	*Children (infants and toddlers):* 4-dose series (0.5 mL each) given intramuscularly at 2, 4, 6, and 12–15 months of age. *Children (unvaccinated, 7 months to 5 years):* 7–11 months, 3 doses (0.5 mL) intramuscularly; 12–23 months, 2 doses (0.5 mL each) intramuscularly; 24 months through 5 years, 1 dose (0.5 mL) intramuscularly. Doses are at least 4 weeks apart. *Children and adults (≥6 years):* 1 dose (0.5 mL) intramuscularly.
Inactivated poliovirus vaccine (IPOL)	Active immunization of infants (as young as 6 weeks of age), children, and adults for the prevention of poliomyelitis caused by poliovirus types 1, 2, and 3	*Children:* 3 doses administered intramuscularly or subcutaneously 8 weeks apart at ages 2, 4, and 6–18 months. The first immunization may be administered as early as 6 weeks of age. Booster dose is administered at 4–6 years of age. *Adults:* 2 0.5 mL doses, given intramuscular or subcutaneously at a 1- to 2-month interval and a third dose given 6–12 months later.
Rotovirus vaccine (Rotarix, RotaTeq)	Indicated for the prevention of rotavirus gastroenteritis caused by G1 and non-G1 types	*Children:* 2-dose (1.5 mL) series orally beginning at 6 weeks of age at an interval of at least 4 weeks between first and second dose. The dose series should be completed by 24 weeks of age; *or* 3-dose (1.5 mL) series orally starting at 6–12 weeks of age with subsequent doses at 4- to-10-week intervals and completed no later than 32 weeks of age.
Varicella vaccine (Varivax)	Active immunization for the prevention of varicella in clients 12 months of age and older	*Children (12 months–12 years):* Initial dose: 0.5 mL intramuscularly at 12–15 months of age but may be given any time through age 12; second dose administered at 4–6 years of age; at least 3 months should elapse between doses. *Teens and adults (≥13 years):* 2 doses (0.5 mL each) administered intramuscularly at least 4 weeks apart.

TABLE 6.1 **Common Recommended Vaccines** (sources: https://dailymed.nlm.nih.gov/dailymed/; https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html#note-mmr)

Name	Indications for Use	Recommended Routes, Dosages, and Time
Zoster vaccine (Shingrix)	Indicated for prevention of herpes zoster (HZ) (shingles): in adults aged 50 years and older and in adults aged 18 years and older who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy	*Adults:* 0.5 mL administered intramuscularly 2–6 months apart. *For clients who are or will be immunodeficient or immunosuppressed and who would benefit from a shorter vaccination schedule:* First dose at month 0 followed by a second dose administered 1–2 months later.
Diphtheria, tetanus toxoid, and acellular pertussis vaccine (DtaP [diphtheria, tetanus, and acellular pertussis vaccine] given to infants and young children; tDaP [tetanus, diphtheria, and acellular pertussis], a booster shot given to older children, adolescents, and adults) (Adacel, Daptacel)	Indicated for active immunization against diphtheria, tetanus, and pertussis as a 5-dose series in infants and children 6 weeks through 6 years of age (prior to seventh birthday)	*DtaP: Children:* 5-dose series (0.5 mL each) intramuscularly at 2, 4, and 6 months of age at intervals of 6–8 weeks, at 15–20 months of age, and at 4–6 years of age. *tDaP (booster)*: 0.5 mL administered intramuscularly 5 years or more after the last dose of DtaP or 5 years of more after a dose of tetanus toxoid adsorbed (Td). A second dose may be administered 8 years or more after the first dose or tDaP.
COVID-19 vaccine, mRNA (Comirnaty, Spikevax)	Indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in clients 12 years of age and older	*For Comirnaty: ≥12 years:* 2 doses (0.3 mL each) intramuscularly 3 weeks apart. *For Spikevax*: *≥18 years:* 2 doses (0.5 mL each) intramuscularly 1 month apart. Booster doses as recommended per season.

TABLE 6.1 Common Recommended Vaccines (sources: https://dailymed.nlm.nih.gov/dailymed/; https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html#note-mmr)

Adverse Effects and Contraindications

Vaccines are generally safe and effective in preventing infectious diseases (CDC, 2023b). However, like any medical intervention, they can have adverse effects. It is important to remember that the benefits of vaccination far outweigh the risks for most people. Vaccine adverse effects commonly involve local and systemic reactions.

Local reactions including tenderness, erythema, induration, and swelling at injection site. Systemic reactions include fever, irritability, drowsiness, anorexia, and vomiting. Other reactions include anaphylactic reactions, such as urticaria and angioedema, as well as nervous system reactions such as convulsions and syncope.

Contraindications to vaccines include hypersensitivity to the vaccine or any of its constituents.

International Travel Considerations

When planning international travel, it is important for clients to consider the possible health risks and ensure all vaccinations are up to date. Vaccines protect against many infectious diseases such as typhoid, yellow fever, hepatitis A and B, meningitis, measles, mumps, rubella, and polio (WHO, n.d.). Some countries may require proof of certain vaccinations for entry. Clients should allow enough time for multiple doses or immunity to develop. An International Certificate of Vaccination may be required by clients traveling abroad.

Clients should consider personal health factors and consult a health care provider before getting vaccinated. Practicing good hygiene and taking preventative measures against foodborne and waterborne illnesses and insect-

borne diseases assists in decreasing risk factors for diseases. It is essential for clients to plan and prioritize immunizations to ensure a safe and healthy travel experience. Consulting a travel health specialist can provide valuable guidance.

CLINICAL TIP

Vaccine Administration

Administration of vaccinations should follow appropriate precautions to minimize risk for disease exposure and spread. The nurse should cleanse their hands with an alcohol-based waterless antiseptic hand rub or wash them with soap and water before preparing vaccines for administration and between each client contact. The nurse should draw up vaccines in a designated clean medication area that is not adjacent to areas where potentially contaminated items are placed. Multi-dose vials to be used for more than one client should not be kept or accessed in the immediate client treatment area.

Nursing Implications

The nurse should do the following for clients who are taking vaccines:

- Review the client's medical history and immunization record to assess for allergies and previous vaccinations to identify any contraindications or precautions for the specific vaccine being administered.
- Educate the client about the vaccine's purpose, potential side effects, and benefits to help the client make an informed decision and reduce vaccine hesitancy.
- Confirm informed consent from the client or their legal guardian before administering the vaccine.
- Check the vaccine's storage and handling to verify that the vaccine has been stored at the appropriate temperature and that it is within the expiration date to maintain its potency and efficacy.
- Prepare and administer the vaccine safely following the guidelines for the vaccine, including the appropriate route, dosage, and injection site. Proper aseptic technique should be maintained throughout the procedure to prevent infections and ensure client safety.
- Provide client teaching regarding vaccines and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving a vaccine should:

- Discuss their medical history with the health care provider and discuss the vaccine prior to immunization.
- Report any reaction caused by the vaccine to the health care provider including local reactions such as tenderness, erythema, and swelling at the injection site; systemic reactions such as fever, irritability, drowsiness, and vomiting; anaphylactic reactions such as urticaria and angioedema; and CNS reactions such as convulsions and syncope.
- Ask questions, seek clarification, and fully understand the information provided before giving their consent for vaccination.

The client receiving a vaccine *should not:*

- Withhold information about their medical history or any known allergies to vaccine components.
- Rush through informed consent.
- Disregard post-vaccination care instructions, as these guidelines can help manage potential side effects and ensure a smooth recovery after vaccination.

6.3 Immunosuppressants, Biologics, Monoclonal Antibodies, and Biosimilar Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 6.3.1 Identify the characteristics of immunosuppressants, biologics, monoclonal antibodies, and biosimilar drugs.
- 6.3.2 Explain the indications, actions, adverse reactions, and interactions for immunosuppressant, biologics, monoclonal antibodies, and biosimilar drugs.
- 6.3.3 Describe the nursing implications related to immunosuppressants, biologics, monoclonal antibodies, and biosimilar drugs.
- 6.3.4 Explain the client education related to immunosuppressants, biologics, monoclonal antibodies, and biosimilar drugs.

This section of the chapter will delve into the realm of therapeutic agents used to manage various autoimmune diseases and conditions. **Immunosuppressants** are drugs that suppress the immune system, helping to prevent organ rejection in transplant recipients and manage autoimmune disorders. **Biologic drugs**, including **monoclonal antibodies**, represent a class of medications derived from living organisms that target specific molecules or cells involved in autoimmune processes, offering highly targeted and personalized treatment options. **Biosimilar drugs**, which are biologic medications designed to be highly similar to already approved biologics, provide cost-effective alternatives with comparable efficacy and safety profiles.

Immunosuppressant Drugs

Immunosuppressant is a class of medicines that inhibit or decrease the intensity of the immune response in the body. They are commonly prescribed to clients who have received an organ transplant and those with autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus. While these medications can effectively prevent rejection of transplanted organs and manage symptoms of autoimmune diseases, they also come with potential adverse effects. Clients taking immunosuppressants may be at higher risk for infections, including opportunistic infections that can be life-threatening.

It is important for clients who are taking immunosuppressant drugs to work closely with their health care provider to monitor any potential side effects and receive regular follow-ups. Additionally, steps should be taken to minimize the risk of infection, such as practicing good hygiene and avoiding close contact with sick clients. Overall, while immunosuppressant drugs can be beneficial in certain medical conditions, it is important for clients to weigh the potential benefits against the risks and work closely with their health care provider to ensure safe and effective use.

Glucocorticoids

Glucocorticoids are a steroid hormone produced by the kidneys' adrenal cortexes that regulate metabolism and the immune system. They have anti-inflammatory and immunosuppressive effects, making them essential in treating inflammatory and autoimmune disorders. Commonly used synthetic glucocorticoids include prednisone and dexamethasone. Glucocorticoids are typically reserved for short-term or last-resort use due to potential toxic effects. Careful tapering is necessary to address potential rebound symptoms resulting from prolonged use (see Table 6.2 for dosing information and Hypothalamus, Pituitary, and Adrenal Disorder Drugs for additional information on glucocorticoids).

Azathioprine

Azathioprine is an immunosuppressant used to treat autoimmune diseases such as rheumatoid arthritis. Azathioprine works by suppressing the immune system, reducing inflammation, and preventing tissue damage. Long-term use has been associated with an increased risk of certain types of cancer. Regular blood tests, such as a complete blood cell count to detect bone marrow suppression or infection, liver function tests to ensure no abnormal liver function is occurring, and serum creatinine to assess proper kidney function, may also be necessary to ensure that the medication is not causing any adverse or harmful effects on the body. See Table 6.3 for additional information on azathioprine.

Mycophenolate

Mycophenolate (also referred to as mycophenolic acid) is an immunosuppressive drug used to prevent organ

rejection in clients who have undergone organ transplantation, such as kidney, heart, or liver transplants. It works by inhibiting the proliferation of T and B immune cells, thus suppressing the immune system's response against the transplanted organs. Mycophenolic acid is commonly used in combination with other immunosuppressants to maintain the function of the transplanted organ and prevent rejection episodes.

Table 6.2 lists common immunosuppressants and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Prednisone	Dosage requirements are variable and individualized based on disease and response of the client; 5–60 mg orally daily. In situations of less severity, lower doses will generally suffice, while in select clients, higher initial doses may be required.
Dexamethasone (Decadron)	Dosage requirements are variable and individualized based on disease and response of the client; 0.75–9 mg orally daily.
Azathioprine (Imuran)	*For rheumatoid arthritis:* 1 mg/kg (50–100 mg) orally given as a single dose or twice daily. The dose may be increased, beginning at 6–8 weeks and thereafter in 4-week intervals. Increments should be 0.5 mg/kg orally daily, up to a maximum dose of 2.5 mg/kg orally per day if there are no serious toxicities and if initial response is unsatisfactory. *For renal homotransplantation:* Dosing is individualized and based on requirements to prevent rejection and minimize toxicity. Initial dose is 3–5 mg/kg orally daily, beginning at the time of transplant, with dose reduction to maintenance levels of 1–3 mg/kg orally daily.
Mycophenolate (Cellcept)	*Children with a BSA 1.25m^2 to <1.5 m^2*: 750 mg orally twice daily (1.5 g total daily dose). *Children with a BSA ≥1.5 m^2*: 1 g orally twice daily (2 g total daily dose). *Adults:* 1.5 g orally twice daily (total daily dose of 3 g).

TABLE 6.2 **Drug Emphasis Table: Immunosuppressants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects for glucocorticoids include weight gain, increased appetite, mood swings, insomnia, fluid retention, and elevated blood sugar levels. Long-term use can lead to more severe adverse effects, such as osteoporosis, high blood pressure, cataracts, and adrenal insufficiency. Contraindications include systemic fungal infections and live virus vaccines.

Azathioprine adverse effects include nausea, vomiting, diarrhea, and a higher risk of infections due to immune suppression. More severe adverse effects include bone marrow suppression, pancreatitis, and liver toxicity. Contraindications include hypersensitivity to the drug or any of its components and in clients with a genetic deficiency of enzyme TPMT (thiopurine methyltransferase).

Mycophenolate adverse effects include gastrointestinal disturbances (nausea, diarrhea), headaches, and an increased susceptibility to infections. It may also be associated with bone marrow suppression and increased risk of birth defects, making it contraindicated during pregnancy.

Table 6.3 is a drug prototype table for immunosuppressants and antimetabolites featuring azathioprine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects and contraindications.

Drug Class Immunosuppressant, antimetabolite **Mechanism of Action** Inhibits DNA synthesis by disrupting the replication and proliferation of T and B immune cells	**Drug Dosage** *For rheumatoid arthritis:* 1 mg/kg (50–100 mg) orally given as a single dose or twice daily. The dose may be increased, beginning at 6–8 weeks and thereafter in 4-week intervals. Increments should be 0.5 mg/kg orally daily, up to a maximum dose of 2.5 mg/kg orally per day if there are no serious toxicities and if initial response is unsatisfactory. *For renal homotransplantation:* Dosing is individualized and based on requirements to prevent rejection and minimize toxicity. Initial dose is 3–5 mg/kg orally daily, beginning at the time of transplant, with dose reduction to maintenance levels of 1–3 mg/kg orally daily.
Indications Management of active rheumatoid arthritis Prevention of rejection in renal homotransplantation **Therapeutic Effects** Decreases inflammation Suppresses the immune response	**Drug Interactions** Alkylating agents Xanthine oxidase inhibitors Febuxostat Aminosalicylates Angiotensin-converting enzyme (ACE) inhibitors Warfarin Ribavirin **Food Interactions** No significant interactions
Adverse Effects Leukopenia/thrombocytopenia/anemia Nausea/vomiting Fever Arthralgias/myalgias Reduction in sperm Hepatotoxicity Increased risk of infection Skin rash Alopecia	**Contraindications** Hypersensitivity Pregnancy and/or breastfeeding Caution: May increase risk of malignancy in clients previously treated with alkylating agents such as cyclophosphamide

TABLE 6.3 **Drug Prototype Table: Azathioprine** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Azathioprine

The use of azathioprine increases the risk of malignancy in humans, including post-transplant lymphoma and hepatosplenic T-cell lymphoma.

Mycophenolic Acid

The use of mycophenolic acid increases the risk of fetal toxicity (resulting in pregnancy loss or congenital malformations), malignancies (lymphomas and skin), and susceptibility to bacterial, viral, fungal, protozoal, and opportunistic infections.

Biologic Drugs and Monoclonal Antibodies

Biologic drugs, also known as *biologics*, are a class of medications derived from living sources such as cells, proteins, or tissues. They are used to treat various medical conditions, particularly autoimmune rheumatic diseases,

and certain types of cancer (American Cancer Society, 2018; Drosos et al., 2021). Biologics are different from traditional chemical-based drugs because of their complex structure and the process used to manufacture them, which involves biotechnology and genetic engineering techniques.

Monoclonal antibodies are a type of biologic drug. They are engineered in the laboratory to target and bind to specific molecules or cells in the body, thus exerting precise and targeted effects (American Cancer Society, 2018). Monoclonal antibodies are designed to mimic the immune system's natural ability to recognize and attack foreign invaders, such as bacteria, viruses, and cancer cells. These antibodies can be used to block certain pathways involved in disease processes, modulate immune responses, or deliver drugs directly to specific cells or tissues.

Both biologic drugs and monoclonal antibodies have revolutionized the treatment of various medical conditions, providing more personalized and effective therapeutic options for clients with complex and difficult-to-treat diseases. However, due to their complex manufacturing process and targeted actions, these medications can be relatively expensive compared to traditional drugs. Additionally, some clients may experience immune-related side effects, and close monitoring is often required during treatment.

Adalimumab

Adalimumab is a monoclonal antibody that targets and inhibits the action of tumor necrosis factor-alpha (TNF-alpha), a cytokine involved in inflammation. By blocking TNF-alpha, adalimumab reduces inflammation and alleviates symptoms associated with various autoimmune diseases. See Table 6.4 for dosing information.

Etanercept

Etanercept is another TNF inhibitor that acts as a soluble TNF receptor, binding to and neutralizing TNF-alpha. Like adalimumab, etanercept dampens the inflammatory response and provides relief from autoimmune-related inflammation. See Table 6.5 for additional information.

Infliximab

Infliximab is a chimeric monoclonal antibody that targets TNF-alpha, effectively neutralizing its activity. Infliximab is often used in conditions such as rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, and inflammatory bowel diseases to manage inflammation and improve quality of life. See Table 6.4 for dosing information.

Rituximab

Rituximab is a monoclonal antibody that targets a specific protein known as CD20 found on the surface of B cells. It is primarily used to treat certain types of non-Hodgkin's lymphoma and chronic lymphocytic leukemia. Rituximab works by binding to CD20-positive B cells, leading to the destruction and reduction in cancerous cell growth. It is also used to treat certain autoimmune diseases like rheumatoid arthritis and systemic lupus erythematosus. See Table 6.4 for dosing information.

Bevacizumab

Bevacizumab (Avastin) is a monoclonal antibody that targets vascular endothelial growth factor (VEGF). It is used to treat various types of cancer, including colorectal cancer, lung cancer, kidney cancer, and glioblastoma multiforme (a type of brain tumor). By inhibiting VEGF, bevacizumab disrupts the formation of new blood vessels that tumors need to grow and spread, ultimately slowing down tumor growth and improving outcomes.

Table 6.4 lists common biologic drugs and monoclonal antibodies and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Adalimumab (Humira)	*RA, AS, PsA 10–<15 kg:* 10 mg subcutaneously every other week. *RA, AS, PsA 15–<30 kg:* 20 mg subcutaneously every other week. *RA, AS, PsA ≥30 kg:* 40 mg subcutaneously every other week.
Etanercept (Enbrel)	*Adult RA, AS, PsA:* 50 mg subcutaneously weekly. *Adult PsO:* Starting dose 50 mg subcutaneously twice weekly for 3 months. Maintenance dose: 50 mg subcutaneously once weekly.
Infliximab (Remicade)	5 mg/kg given as an intravenous induction regimen at 0, 2, and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter.

TABLE 6.4 **Drug Emphasis Table: Biologic Drugs and Monoclonal Antibodies** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Rituximab (Rituxan)	*First infusion:* 50 mg/hour intravenously. In the absence of infusion toxicity, increase infusion rate by 50 mg/hour increments every 30 minutes, to a maximum of 400 mg/hour. *Subsequent infusion:* Initiate infusion at a rate of 100 mg/hr. In the absence of infusion toxicity, increase rate by 100 mg/hour increments at 30-minute intervals, to a maximum of 400 mg/hour.
Bevacizumab (Avastin)	Dosing is individualized and depends on the type of cancer being treated and the combination of other chemotherapy drugs being used. 5–15 mg/kg intravenously every 2–3 weeks.

TABLE 6.4 **Drug Emphasis Table: Biologic Drugs and Monoclonal Antibodies** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects of biologic drugs and monoclonal antibodies include increased risk of infections (bacterial, viral, fungal, and opportunistic infections), injection site reactions (erythema, itching, pain, and swelling), diarrhea, rash, pruritis, anemia, leukopenia, thrombocytopenia, congestive heart failure, lymphomas and certain types of skin cancer (melanoma and non-melanoma), convulsions, headache, interstitial lung disease, cutaneous vasculitis, Stevens–Johnson syndrome, and toxic epidermal necrolysis. Contraindications include hypersensitivity to the drug or any of its components, active infection, sepsis, pregnancy, and breastfeeding.

Table 6.5 is a drug prototype table for biologic, TNF inhibitors featuring etanercept. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Biologic, TNF inhibitor **Mechanism of Action** Blocks the binding of TNF-α and TNF-β (lymphotoxin-α [LT-α]) to cell surface TNF receptors, resulting in the inactivation of TNF's biological effects	**Drug Dosage** *Adult RA, AS, PsA:* 50 mg subcutaneously weekly. *Adult PsO:* Starting dose 50 mg subcutaneously twice weekly for 3 months. Maintenance dose: 50 mg subcutaneously once weekly.
Indications Rheumatoid arthritis Polyarticular juvenile idiopathic arthritis Psoriatic arthritis Ankylosing spondylitis Plaque psoriasis **Therapeutic Effects** Decreases inflammation Suppresses the immune response	**Drug Interactions** Live vaccines Anakinra Cyclophosphamide Sulfasalazine **Food Interactions** No significant interactions
Adverse Effects Infections, including viral, bacterial, and fungal infection Injection site reactions (erythema, itching, pain, swelling) Diarrhea Rash Pruritis Hematologic (anemia, leukopenia, thrombocytopenia) Congestive heart failure Hepatotoxicity Lymphomas, melanoma, skin cancers, and Merkel cell carcinoma Convulsions Paresthesia Headache Interstitial lung disease Cutaneous vasculitis Stevens–Johnson syndrome Toxic epidermal necrolysis	**Contraindications** Hypersensitivity Active infection or sepsis Pregnancy and/or breastfeeding Caution: May increase risk of malignancy and can increase the risk of reactivating latent tuberculosis

TABLE 6.5 **Drug Prototype Table: Etanercept** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Biologics and Monoclonal Antibodies

Biologic drugs and monoclonal antibodies increase the risk for infections including active tuberculosis and invasive fungal infections as well as bacterial, viral, and other opportunistic infections. They also can increase the risk for certain cancers including lymphomas, melanoma, non-melanoma skin cancer, and Merkel cell carcinoma.

Biosimilar Drugs

Biosimilar drugs are a type of biologic medication that is highly similar to an already approved reference biologic, also known as the original biologic or reference product. Biosimilars are designed to have similar efficacy, safety, and quality as the reference product (American Cancer Society, 2018; U.S. Food and Drug Administration, 2023).

They are developed to be equivalent in terms of structure, biological activity, and clinical effects.

Unlike generic versions of traditional chemical-based drugs, which are identical to their reference products, biosimilars are not exact copies due to the complexity of biologics and the variability in the manufacturing process. Biosimilars undergo rigorous testing and comparison to the reference product to ensure they are highly similar and have no clinically meaningful differences in terms of safety and efficacy.

Biosimilars offer an opportunity to increase access to effective biologic treatments at potentially lower costs compared to the reference products. They play a crucial role in promoting competition and driving down prices, making biologic therapies more affordable for clients and health care systems.

Regulatory authorities, such as the U.S. Food and Drug Administration (FDA), have established robust guidelines for the approval of biosimilars, ensuring they meet stringent standards for quality, safety, and efficacy (American Cancer Society, 2018). This regulatory framework ensures that clients can have confidence in the safety and effectiveness of biosimilar medications.

Pegfilgrastim

Pegfilgrastim is a medication used to reduce the risk of infection in clients undergoing certain cancer treatments, such as chemotherapy, that may cause a decrease in the body's white blood cell count. It is a long-acting form of filgrastim, a synthetic version of a natural protein called granulocyte-colony stimulating factor (G-CSF).

Pegfilgrastim stimulates the bone marrow to increase white blood cell production, particularly neutrophils, which are essential for fighting infections. By increasing the white blood cell count, pegfilgrastim helps to reduce the likelihood of severe infections during cancer treatment. See Table 6.7 for additional information.

Table 6.6 lists common biosimilar drugs along with the typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Bortezomib (Velcade)	Dosage requirements are variable and individualized based on disease and response of the client. 1.3 mg/m^2 intravenously at a concentration of 1 mg/mL in 3- to 5-second bolus.
Pegfilgrastim (Neulasta)	*For clients receiving myelosuppression chemotherapy:* 6 mg subcutaneously once per chemotherapy cycle. *For clients with hematopoietic subsyndrome of acute radiation syndrome:* 2 doses 6 mg each subcutaneously 1 week apart.

TABLE 6.6 Drug Emphasis Table: Biosimilar Drugs (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of bortezomib include GI effects (nausea, vomiting, diarrhea, constipation, fatigue, weakness, peripheral neuropathy, thrombocytopenia, anemia, neutropenia, fever, chills, and skin reaction). Contraindications include hypersensitivity to the drug or any of its components, severe liver impairment, and pregnancy and/or breastfeeding.

Adverse effects of pegfilgrastim also include bone pain, pain in the arms and legs, headache, fatigue and weakness, nausea, and injection site reactions (pain, erythema, and swelling). Contraindications include hypersensitivity to the drug or any of its components, pregnancy, and breastfeeding.

Table 6.7 is a drug prototype table for biosimilar drugs featuring pegfilgrastim. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Biosimilar, granulocyte-colony stimulating factors (G-CSFs) **Mechanism of Action** Binds to the precursor receptor cells on the surface of bone marrow cells, thereby signaling the bone marrow to increase the production and release of neutrophils into the bloodstream	**Drug Dosage** *For clients receiving myelosuppression chemotherapy:* 6 mg subcutaneously once per chemotherapy cycle. *For clients with hematopoietic subsyndrome of acute radiation syndrome:* 2 doses 6 mg each subcutaneously 1 week apart.
Indications Clients with cancer receiving myelosuppression chemotherapy Clients with hematopoietic subsyndrome of acute radiation syndrome **Therapeutic Effects** Increases production of white blood cells, particularly neutrophils	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Splenic rupture Bone pain Pain in extremities Headache Fatigue Nausea Injection site reactions (pain, erythema, and swelling)	**Contraindications** Hypersensitivity Pregnancy and/or breastfeeding

TABLE 6.7 **Drug Prototype Table: Pegfilgrastim** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking immunosuppressants, biologics, monoclonal antibodies, and biosimilar drugs:

- Review the client's medical history to assess allergies and contraindications or potential drug interactions with current medications.
- Monitor complete blood counts for leukopenia, thrombocytopenia, and anemia; liver function tests for hepatotoxicity; renal functions tests for nephrotoxicity; and lipids for elevated lipid levels.
- Evaluate the client's tuberculosis (TB) status prior to administering biologic drugs, as they can increase the risk of reactivating latent tuberculosis.
- Educate the client about the drug's purpose, potential side effects, and benefits to help the client make an informed decision about the treatment plan.
- Ensure proper administration technique including the appropriate route, dosage, and injection site. Maintain proper aseptic technique throughout the procedure to prevent infections and ensure client safety.
- After administration, closely monitor the client for any immediate adverse reactions, such as allergic responses or infusion-related reactions. Vital signs, signs of infection, and changes in the client's condition should be regularly assessed, and any concerns should be promptly reported to the health care provider.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an immunosuppressant, biologic drug, monoclonal antibody, or biosimilar drug should:

- Choose an injection site as recommended by the health care provider, avoiding areas that are bony,

bruised, sore, red, scarred, or hard.
- Cleanse the injection area with an alcohol swab/pad and let dry for 30 seconds prior to administering the drug.
- Dispose of needles in an FDA-approved sharps disposal container after use.
- Keep a journal of symptoms and note improved or worsening symptoms.
- Practice good hygiene and avoid contact with sick individuals to decrease the risk of infection.
- Report symptoms of fever, chills, sore throat, and skin rash to the health care provider because these may indicate an adverse reaction to the drug.
- Attend all appointments, undergo recommended blood tests, and report any changes or concerns to the health care provider.

The client taking an immunosuppressant, biologic drug, monoclonal antibody, or biosimilar drug *should not:*

- Dispose of needles or sharps container in the household trash.
- Reuse needles.
- Stop taking the drug unless directed by the health care provider.
- Get a live vaccine such as measles, mumps, and rubella (MMR) or oral polio vaccine (OPV), as this increases the risk of developing the disease from the immunization.

6.4 Introduction to the Inflammatory Response and Anti-inflammatory Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:
- 6.4.1 Describe the pathophysiology of inflammation.
- 6.4.2 Discuss the five cardinal signs of inflammation.
- 6.4.3 Identify the etiology and diagnostic studies related to inflammation.
- 6.4.4 Identify the characteristics of drugs used to treat inflammation.
- 6.4.5 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat inflammation.
- 6.4.6 Describe the nursing implications of drugs used to treat inflammation.
- 6.4.7 Explain the client education related to drugs used to treat inflammation.

Inflammation, the body's complex response to harmful stimuli, plays an important role in the immune system's defense against injury and infection. This section of the chapter explores mechanisms for inflammation and drugs used to treat inflammation.

Inflammation

Inflammation is a fundamental biological response that the body activates in response to harmful stimuli, such as pathogens, tissue injury, or irritants. It is a crucial part of the immune system's defense mechanism, designed to protect the body and initiate the healing process. Inflammation involves a series of intricate events and interactions among cells, chemicals, and blood vessels. When tissues are damaged or infected, various immune cells are recruited to the site of injury or infection (Chen et al., 2018; Hannoodee & Nasuruddin, 2022). The key players in the inflammatory response include:

- *Mast cells:* These cells are present in connective tissues and release substances such as histamine, which trigger blood vessels to dilate and become more permeable, leading to increased blood flow and leakage of fluid into the affected area.
- *White blood cells (leukocytes):* Neutrophils and macrophages are the primary types of leukocytes involved in the inflammatory response. They migrate to the site of injury or infection to engulf and destroy invading pathogens and damaged cells.
- *Cytokines:* These are signaling molecules that help regulate the immune response and mediate communication between different cells. Pro-inflammatory cytokines, such as interleukin-1 (IL-1) and tumor necrosis factor-alpha (TNF-α), play a central role in initiating and amplifying the inflammatory process.
- *Chemokines:* These are a subgroup of cytokines that attract immune cells to the site of inflammation,

promoting their migration and recruitment (Chen et al., 2018; Hannoodee & Nasuruddin, 2022; Patel & Mohiuddin, 2023).

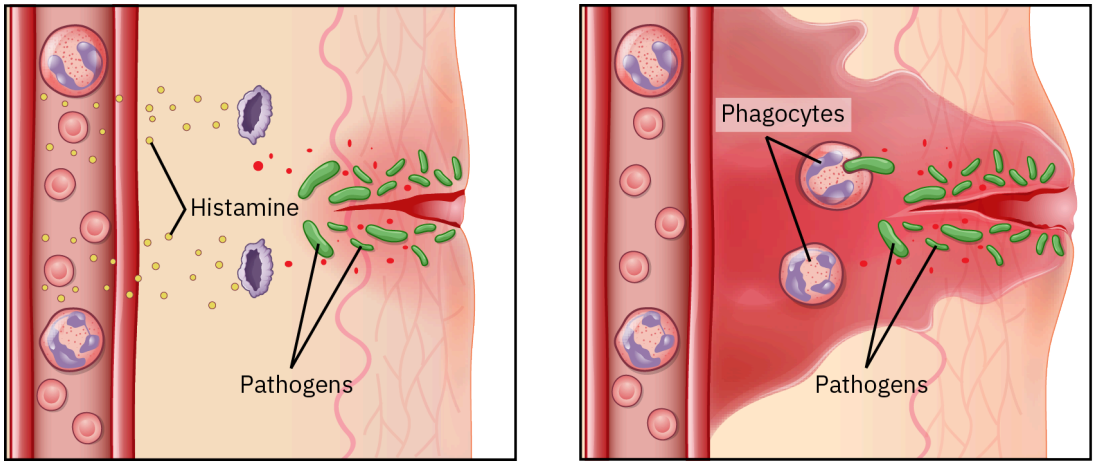
There are five cardinal signs of inflammation that were first described by the Roman encyclopedist Celsus in the 1st century AD and are still widely recognized as classic indicators of an inflammatory response in the body (Cavaillon, 2021). These are (Chen et al., 2018; Hannoodee & Nasuruddin, 2022):

- *Redness (rubor):* The affected area becomes red due to increased blood flow and dilation of blood vessels in response to inflammation.
- *Swelling (tumor):* Swelling occurs as fluid and immune cells accumulate at the site of inflammation.
- *Heat (calor):* Inflammation leads to increased blood flow and metabolic activity in the affected area, resulting in elevated temperature and warmth.
- *Pain (dolor):* Inflammatory mediators sensitize nerve endings in the affected region, leading to pain.
- *Loss of function (functio laesa):* In more severe cases of inflammation, the affected area may lose some or all of its normal function. This can occur due to the damage caused by the inflammation or the body's protective response to limit further harm.

Pathophysiology

The body's **inflammatory response** is a complex and coordinated reaction aimed at defending against harmful stimuli and promoting tissue repair (Hannoodee & Nasuruddin, 2022). When tissues are damaged, injured, or infected, various immune cells and chemical mediators work together to initiate and regulate the inflammatory process. The response can be triggered by various factors, including pathogens (e.g., bacteria, viruses), physical injury, toxins, or autoimmune reactions. The inflammatory response (see Figure 6.4) presents as follows:

- *Recognition of harmful stimuli:* The process begins when the body detects a threat, such as a pathogen or tissue injury. Immune cells, particularly macrophages, recognize these harmful stimuli through pattern recognition receptors.
- *Release of chemical mediators:* Upon recognition of the threat, immune cells release signaling molecules called cytokines, such as interleukins and TNF-α, which trigger the cascade of events that lead to inflammation.
- *Vasodilation:* Cytokines and other chemical mediators cause blood vessels in the affected area to dilate, leading to increased blood flow and allowing more immune cells, antibodies, and nutrients to reach the site of injury or infection.
- *Increased vascular permeability:* The cytokines increase the permeability of blood vessel walls, leading to the leakage of fluid and proteins into the surrounding tissues, which contributes to the swelling, redness, and warmth.
- *Migration of immune cells:* Chemokines attract immune cells, particularly neutrophils and monocytes.
- *Phagocytosis and immune response*: Neutrophils and macrophages engulf and destroy invading pathogens, dead cells, and debris through a process called phagocytosis. This helps contain the infection and clear away damaged tissues.
- *Activation of the adaptive immune system:* As the inflammatory response progresses, dendritic cells, another type of immune cell, process and present antigens from the pathogens to T and B lymphocytes. This leads to the activation of the adaptive immune system, which provides a more specific and targeted response to infection.
- *Resolution and tissue repair*: As the threat is neutralized and the tissue damage begins to heal, the body releases anti-inflammatory cytokines, such as interleukin-10 (IL-10), which promote the resolution of inflammation. Immune cells shift their focus to tissue repair and regeneration.



1 Mast cells detect injury to nearby cells and release histamine, initiating inflammatory response.

2 Histamine increases blood flow to the wound sites, bringing in phagocytes and other immune cells that neutralize pathogens. The blood influx causes the wound to swell, redden, and become warm and painful.

FIGURE 6.4 This diagram illustrates the inflammatory response, which results in warmth, redness, pain, and swelling as well as the recruitment of phagocytes. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The inflammatory response is a highly regulated process that aims to eliminate the threat, initiate healing, and restore tissue function. However, an exaggerated or dysregulated inflammatory response can lead to chronic inflammation and contribute to various diseases. Anti-inflammatory drugs are used to control and modulate this response, providing relief and preventing further tissue damage in certain conditions.

Etiology and Diagnostic Testing

Factors that trigger the inflammatory response in the body can arise from various sources, including infections (bacterial, viral, fungal, and parasitic), physical injury to tissue (trauma, burns), autoimmune disorders (rheumatoid arthritis, systemic lupus erythematosus), allergic reactions, irritants, and chronic conditions such as chronic obstructive pulmonary disorders (COPD) and peripheral vascular disorders (PVD).

Diagnostic and lab studies are essential for diagnosing and assessing inflammation. Some common tests and investigations include:

- *Complete blood count (CBC) with differential:* This test provides information about the number and types of blood cells, including white blood cells (WBCs). An increased WBC count, particularly neutrophils, can indicate an inflammatory response.
- *C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR):* These blood tests measure markers of inflammation. Elevated levels of CRP or an accelerated ESR suggest the presence of inflammation in the body.
- *Blood cultures:* If an infection is suspected as the cause of inflammation, blood cultures may be performed to identify the specific microorganism responsible.
- *Imaging studies:* X-rays, ultrasounds, CT scans, or MRIs can help visualize inflamed tissues and identify the extent of inflammation or structural damage.
- *Biopsy:* In some cases, a tissue sample may be obtained through a biopsy to determine the cause and severity of inflammation.
- *Autoantibody testing:* For suspected autoimmune disorders, specific autoantibody tests can be conducted to identify abnormal immune responses against the body's own tissues.
- *Allergy testing:* In cases of allergic inflammation, skin tests or blood tests can help identify specific allergens responsible for the allergic response.

The combination of clinical evaluation, medical history, and appropriate diagnostic tests helps health care providers diagnose the presence of inflammation, identify its underlying cause, and develop an effective treatment plan to address the condition.

Inflammation versus Infection

Inflammation and infection are related but distinct concepts in the context of the body's response to harmful stimuli. Inflammation is a general physiological response of the body to tissue injury, irritation, or foreign substances. It is a part of the body's immune defense mechanism and plays a vital role in protecting and healing tissues. Inflammation can be triggered by various factors, such as physical injury, exposure to irritants, autoimmune reactions, or the presence of pathogens like bacteria or viruses. When tissues are damaged or perceived to be under threat, immune cells and chemical mediators are recruited to the affected site, leading to the characteristic symptoms of inflammation, including redness, swelling, heat, and pain. The inflammatory response aims to eliminate the source of injury or infection, clear away damaged cells and debris, and initiate tissue repair (Chen et al., 2018; Hannoodee & Nasuruddin, 2022).

Infection, on the other hand, specifically refers to the invasion and colonization of the body by harmful microorganisms such as bacteria, viruses, or other microbes (CDC, 2016). When pathogens enter the body, they can multiply and cause damage to tissues, leading to illness. Infections can occur in various parts of the body, such as the respiratory tract, urinary tract, gastrointestinal system, or bloodstream. The body responds to infections by initiating an inflammatory response as part of its immune defense mechanism. Infections may or may not cause obvious symptoms of inflammation, depending on the type and location of the infection and the client's immune response. While not all inflammation is caused by infections, infections frequently lead to an inflammatory response.

Anti-inflammatory Drugs

Anti-inflammatory drugs are a classification of drugs used to reduce inflammation, relieve pain, and alleviate fever (Ghlichloo & Gerriets, 2023). These drugs work by inhibiting the production of certain enzymes called cyclooxygenase (COX), which are involved in the synthesis of prostaglandins, hormone like-substances that play a role in the inflammatory response.

Nonsteroidal Anti-inflammatory Drugs

Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit both COX-1 and COX-2 enzymes. COX-1 and COX-2 are enzymes involved in the production of prostaglandins, which are signaling molecules that regulate inflammation and various physiological processes. COX-1 is constitutively present in many tissues and plays a role in maintaining normal bodily functions, such as protecting the stomach lining and regulating blood clotting. COX-2 is induced during inflammation and is primarily responsible for generating prostaglandins that contribute to pain, inflammation, and other responses associated with injury and inflammation. The inhibition of these enzymes helps to decrease inflammation, pain, and fever. These drugs are for short-term use, and many can be found over the counter (OTC). Several subclassifications of NSAIDs are explored in the subsequent sections.

Salicylates

Salicylates are a group of chemical compounds that contain a salicylate acid backbone. The most common and well-known salicylate is acetylsalicylic acid, also known as aspirin. Salicylates can be found in various plants, including fruits (such as berries), vegetables (such as spinach), and herbs (such as peppermint). Salicylates are commonly used to alleviate pain, reduce inflammation, and lower fever, making them effective for various conditions, including headaches, arthritis, and minor injuries. See Table 6.8 for dosing information and Pain Response Drugs for additional information on salicylates.

Aspirin also has anti-platelet properties that are unrelated to its anti-inflammatory properties. At low doses, aspirin irreversibly inhibits the enzyme cyclooxygenase-1 (COX-1) in platelets, which are specialized blood cells involved in blood clotting, thereby inhibiting platelet aggregation and blood clot formation (see Anticoagulant, Antiplatelet, and Thrombolytic Drugs for additional information on aspirin as an antiplatelet).

Phenylacetic Acid Derivatives

Phenylacetic acid derivatives are a class of chemical compounds that have a phenylacetic acid structure. These derivatives are often found in medications and are used for various therapeutic purposes. Like salicylates, phenylacetic acid derivatives inhibit the enzyme cyclooxygenase, thereby decreasing inflammation. They also act as an antipyretic and analgesic to alleviate pain. Common phenylacetic acid derivatives include diclofenac and indomethacin. See Table 6.8 for dosing information.

Propionic Acid Derivatives

Propionic acid derivatives have a propionic acid base in their chemical structure. They also inhibit the enzyme COX, thereby decreasing inflammation, relieving pain, and reducing fever. Common propionic acid derivatives include ibuprofen and naproxen sodium. See Table 6.8 for dosing information and Pain Response Drugs for additional information on these drugs.

Oxicams

Oxicams are a class of NSAIDs that share a common chemical structure called "oxicam." These drugs work by inhibiting the enzyme COX, thus decreasing the inflammatory response. Oxicams are used for their anti-inflammatory, analgesic (pain-relieving), and antipyretic (fever-reducing) properties, like other NSAIDs. Common oxicams include meloxicam and piroxicam. See Table 6.8 for dosing information.

COX-2 Inhibitors

COX-2 inhibitors are a specific class of NSAIDs that selectively target and inhibit the cyclooxygenase-2 (COX-2) enzyme. This class of drugs was developed to provide pain relief and anti-inflammatory effects while minimizing some of the gastrointestinal side effects associated with traditional non-selective NSAIDs, which inhibit both COX-1 and COX-2 enzymes. Celecoxib is the only COX-2 inhibitor on the market in the United States. See Table 6.9 for additional information.

Table 6.8 lists common nonsteroidal anti-inflammatory drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Salicylates	
Salicylic acid (aspirin)	Tablet or enteric coated tablet, 1 or 2 325 mg tablets orally every 4 hours while symptoms last.
Phenylacetic Acid Derivatives	
Diclofenac (Voltaren)	*For the relief of osteoarthritis:* 100–150 mg/day orally in divided doses, 50 mg 2 or 3 times a day. *For the relief of rheumatoid arthritis:* 150–200 mg/day orally in divided doses, 50 mg 3 or 4 times a day.
Indomethacin (Indocin, Tivorbex)	*Immediate release:* 25 mg orally 2 or 3 times daily. Increase the daily dosage by 25–50 mg, if required by continuing symptoms, at weekly intervals until a satisfactory response is obtained or until a total daily dose of 150–200 mg is reached. *Extended release:* 75 mg orally once daily.
Propionic Acid Derivatives	
Ibuprofen (Advil)	200 mg orally every 4–6 hours while symptoms persist.
Naproxen sodium (Aleve)	220 mg orally every 8–12 hours while symptoms last. Do not exceed 440 mg in any 8- to 12-hour period; do not exceed 660 mg in a 24-hour period.
Oxicams	
Meloxicam (Mobic)	5 mg orally once daily. May be increased to 10 mg orally in clients who require additional analgesia. Maximum daily dose: 10 mg.
Piroxicam (Feldene)	20 mg orally once daily.
COX-2 Inhibitor	
Celecoxib (Celebrex)	100–200 mg orally twice daily.

TABLE 6.8 **Drug Emphasis Table: Nonsteroidal Anti-inflammatory Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Although NSAIDs are generally well-tolerated, they can have adverse effects and contraindications that clients

should be aware of. It is important to note that the severity and occurrence of adverse effects can vary from person to person, and not everyone will experience all of the listed adverse effects. Common adverse effects of NSAIDs include gastrointestinal issues (stomach pain, heartburn, indigestion, nausea, GI bleeding), headache, dizziness, fluid retention, high blood pressure, renal and liver impairment, and an increased risk of cardiovascular events such as heart attack and stroke.

Contraindications include hypersensitivity to the drug or any of its components; having a history of allergies, asthma, or urticaria (hives) after taking aspirin or other NSAIDs; coronary artery bypass graft (CABG) surgery; and with celecoxib sulfonamide allergy.

Table 6.9 is a drug prototype table for NSAIDs featuring celecoxib. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class NSAID, COX-2 inhibitor **Mechanism of Action** Inhibits prostaglandin synthesis, primarily via inhibition of COX-2	**Drug Dosage** 100–200 mg orally twice daily.
Indications Osteoarthritis Rheumatoid arthritis Ankylosing spondylitis Acute pain Primary dysmenorrhea **Therapeutic Effects** Decreases inflammation and pain	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Abdominal pain Dyspepsia Peripheral edema Dizziness Rash Hepatotoxicity Renal toxicity GI bleeding Thrombocythemia Bronchospasm Photosensitivity	**Contraindications** Hypersensitivity History of allergies, asthma, or urticaria after taking aspirin or other NSAIDs CABG surgery Sulfonamide allergy Caution: May increase risk of cardiovascular thrombotic events and GI bleeding

TABLE 6.9 **Drug Prototype Table: Celecoxib** (source: https://dailymed.nlm.nih.gov/dailymed/)

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NSAIDs

NSAIDs increase the risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use.

NSAIDs also increased the risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Older clients and clients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

Glucocorticoid Drugs

Glucocorticoids, also known as corticosteroids or simply steroids, are a class of anti-inflammatory drugs that mimic the action of naturally occurring hormones produced by the adrenal glands. These hormones, specifically cortisol, play a crucial role in regulating the body's response to stress and inflammation. When used as medication, synthetic glucocorticoids have potent anti-inflammatory effects due to their ability to modify the immune response. See Immunosuppressants, Biologics, Monoclonal Antibodies, and Biosimilar Drugs and Hypothalamus, Pituitary, and Adrenal Disorder Drugs for drug information on glucocorticoids.

Disease-Modifying Antirheumatic Drugs (DMARDs)

Disease-modifying antirheumatic drugs (DMARDs) are a class of medications used primarily to treat autoimmune and inflammatory conditions such as rheumatoid arthritis (Benjamin et al., 2022; Mysler et al., 2021). These drugs work by targeting specific components of the immune system to suppress the abnormal immune reaction responsible for causing inflammation and tissue damage.

DMARDs have immunomodulatory effects, meaning they modify the immune response rather than just providing symptomatic relief. The main goal of DMARDs is to slow down or modify the underlying disease process, reduce joint damage, and improve long-term outcomes for clients with autoimmune diseases. They may take weeks to months to achieve the disease-modifying effects. DMARDs are usually prescribed for long-term use and are considered the ongoing management of autoimmune conditions.

Conversely, non-DMARDs, such as NSAIDs and glucocorticoids, primarily provide symptomatic relief by reducing pain and inflammation. They do not alter the underlying disease process or the progression of the autoimmune condition. Non-DMARDs are often used for short-term and intermittent relief of acute symptoms, especially pain and inflammation. Non-DMARDs are often used in combination with DMARDs for comprehensive autoimmune disease management.

DMARDs can include both biologics and non-biologic drugs (Mysler et al., 2021). The choice of DMARD depends on the specific condition being treated, disease severity, individual response, and potential side effects. Treatment decisions are made in consultation with a health care provider who will tailor the therapy to each client’s unique needs and health status.

Biologic DMARDs

Biologic DMARDs are drugs derived from living cells or organisms. They are typically large, complex molecules produced through biotechnology processes. They target specific components of the immune system to suppress the abnormal immune response seen in autoimmune diseases. Biologic drugs such as adalimumab, etanercept, infliximab, and rituximab are discussed in Immunosuppressants, Biologics, Monoclonal Antibodies, and Biosimilar Drugs.

Non-biologic DMARDs

Non-biologic DMARDs, also known as conventional or synthetic DMARDs, are small-molecule drugs synthesized chemically. They are not derived from living sources and typically have a more general or broader mode of action. They may act on multiple targets within the immune system or inhibit enzymes that play a role in the inflammatory process. For example, methotrexate inhibits an enzyme involved in the synthesis of DNA and RNA, which affects rapidly dividing cells, including immune cells. Common non-biologic DMARDs include methotrexate, sulfasalazine, and gold salts. See Table 6.10 for dosing information and Table 6.11 for additional information on methotrexate.

Table 6.10 lists common non-biologic DMARDs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Methotrexate (Trexall)	7.5 mg orally once weekly with escalation to achieve optimal response. Dosages of more than 20 mg once weekly result in an increased risk of serious adverse reactions, including myelosuppression.
Sulfasalazine (Azulfidine)	*Initial therapy:* 3000–4000 mg orally daily in evenly divided doses with dosage intervals not exceeding 8 hours. *Maintenance therapy:* 2000 mg orally daily.

TABLE 6.10 **Drug Emphasis Table: Non-Biologic Disease-Modifying Antirheumatic Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects for non-biologic DMARDs include nausea/vomiting, diarrhea, abdominal pain, hepatotoxicity, rash, anemia, thrombocytopenia, neutropenia, photosensitivity, elevated blood pressure, hair loss, hypotension, pancreatitis, and with methotrexate, optic neuritis. Contraindications include hypersensitivity to the drug or any of its constituents, pregnancy and/or breastfeeding, myelosuppression, live vaccines, alcohol use, pre-existing bleeding disorders, and in clients who have an active infection. For adverse effects and contraindications for biologic DMARDs, see Immunosuppressants, Biologics, Monoclonal Antibodies, and Biosimilar Drugs in this chapter.

Table 6.11 is a drug prototype table for DMARDs featuring methotrexate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anti-inflammatory, DMARDs, antineoplastic **Mechanism of Action** Inhibits enzyme AICAR transformylase, leading to hindrance in adenosine and guanine metabolism, thereby decreasing inflammation	**Drug Dosage** 7.5 mg orally once weekly with escalation to achieve optimal response. Dosages of more than 20 mg once weekly result in an increased risk of serious adverse reactions, including myelosuppression.
Indications Rheumatoid arthritis Psoriasis Acute lymphoblastic leukemia and non-Hodgkin lymphomas **Therapeutic Effects** Decreases inflammation Suppresses the immune response	**Drug Interactions** Neomycin Antifolate drugs NSAIDs Phenytoin Probenecid Folic acid **Food Interactions** No significant interactions
Adverse Effects Deep vein thrombosis/pulmonary emboli Hypotension Hyperglycemia Optic neuropathy Pancreatitis Anemia Hepatoxicity Osteoporosis Alopecia Hematuria Pulmonary fibrosis Skin necrosis	**Contraindications** Hypersensitivity Pregnancy and/or breastfeeding Myelosuppression Live vaccines Alcohol use Preexisting bleeding disorders Active infection Caution: May cause myelosuppression

TABLE 6.11 **Drug Prototype Table: Methotrexate** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Methotrexate and Gold Salts

Methotrexate can cause embryo-fetal toxicity, including fetal death. For non-neoplastic diseases, methotrexate tablets are contraindicated in pregnancy. For neoplastic diseases, advise clients of childbearing age of the potential risk to a fetus and to use effective contraception.

Serious adverse reactions, including death, have been reported with methotrexate. Closely monitor for adverse reactions of the bone marrow, gastrointestinal tract, liver, lungs, skin, and kidneys. Withhold or discontinue methotrexate tablets as appropriate.

Antimalarial Drugs

Antimalarial drugs are a group of medications primarily used to treat and prevent malaria, a parasitic infection transmitted by mosquito bites. However, some antimalarial drugs have been found to have beneficial effects in the treatment of certain autoimmune diseases due to their immunomodulatory properties.

The exact mechanisms of action of these drugs in autoimmune diseases are not fully understood, but they are believed to modulate the immune response by influencing the function of immune cells and cytokines involved in the inflammatory process (Haładyj et al., 2018). Therefore, they help to control disease activity by decreasing inflammation, slowing joint damage, and preserving joint function, reducing the frequency of flares and improving overall disease management.

The two main antimalarial drugs used in autoimmune disease treatment are hydroxychloroquine and chloroquine. These drugs are known to have anti-inflammatory and immunomodulatory effects, which can help in managing autoimmune conditions.

It is important to note that while antimalarial drugs can be beneficial for some clients with autoimmune diseases, not everyone responds the same way to these medications. The decision to suggest antimalarial drugs as part of the treatment plan is made by a health care professional, who considers the specific autoimmune condition, disease severity, individual response, and potential side effects.

Hydroxychloroquine

Hydroxychloroquine is the more commonly prescribed antimalarial drug for autoimmune disease treatment. It is used to manage conditions such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Hydroxychloroquine works by interfering with the immune response and dampening the activity of certain immune cells. It can help reduce inflammation, slow disease progression, preserve joint function, and improve disease control in some clients with autoimmune disorders. See Table 6.13 for additional information on hydroxychloroquine.

Chloroquine

Chloroquine shares similar properties with hydroxychloroquine. It has been used to treat autoimmune diseases, but its use has decreased due to the availability of hydroxychloroquine, which is considered to have a better safety profile.

Table 6.12 lists common antimalarial drugs with typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Hydroxychloroquine (Plaquenil)	*Initial dosage*: 400–600 mg orally daily. *Chronic dosage:* 200–400 mg orally daily.
Chloroquine (Chloroquine FNA)	500 mg orally once per week on exactly the same day of each week.

TABLE 6.12 **Drug Emphasis Table: Antimalarial Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects of antimalarials used as anti-inflammatories include gastrointestinal issues (nausea,

vomiting, diarrhea, abdominal pain), prolonged QT interval, tachycardia, rash, itching, hepatotoxicity, renal impairment, photosensitivity, visual field disturbances, retinopathy, alopecia, myopathy and muscle weakness, agranulocytosis, and aplastic anemia.

Contraindications include hypersensitivity to the drug or any of its components, preexisting eye conditions such as macular degeneration, preexisting heart conditions such as arrythmias, pregnancy and/or breastfeeding, and liver or renal impairment.

Table 6.13 is a drug prototype table for antimalarial drugs featuring hydroxychloroquine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antimalarial **Mechanism of Action** Inhibits antigen presentation, B- and T-cell activation, and NOX signaling	**Drug Dosage** *Initial dosage*: 400–600 mg orally daily. *Chronic dosage:* 200–400 mg orally daily.
Indications Rheumatoid arthritis Systemic lupus erythematosus Chronic discoid lupus erythematosus Malaria **Therapeutic Effects** Decreases inflammation Suppresses the immune response	**Drug Interactions** Antiarrhythmics Antiepileptics Methotrexate Digoxin Cimetidine Rifampin Praziquantel Antacids Ampicillin **Food Interactions** No significant interactions
Adverse Effects Bone marrow suppression Anemia/thrombocytopenia Prolonged QT interval Tachycardia Pulmonary hypertension Retinopathy/visual field disturbances Nausea/vomiting Fatigue Urticaria Myopathy Headache Seizure Alopecia Hepatotoxicity Renal impairment	**Contraindications** Hypersensitivity Pregnancy and/or breastfeeding Preexisting eye conditions Preexisting heart conditions Liver or renal impairment Caution: May worsen eye conditions such as macular degeneration

TABLE 6.13 **Drug Prototype Table: Hydroxychloroquine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Antigout Drugs

Antigout drugs are a class of medications used to treat gout, a condition caused by the buildup of uric acid crystals in the joints. These drugs work to manage acute gout attacks and prevent future gout flares by reducing the level of uric acid in the body or by alleviating inflammation and pain associated with gout attacks (National Institute for Health and Care Excellence (NICE), 2022).

Although various drugs can be used to treat gout, including glucocorticoids and NSAIDs, this section of the chapter will only discuss the more common drugs used to treat gout (and its inflammatory response): colchicine, allopurinol, and probenecid.

Colchicine

Colchicine is an alkaloid drug derived from the autumn crocus plant. It is used to treat acute gout attacks and can help reduce inflammation and pain in the affected joints. Colchicine works by interfering with the movement of white blood cells to the inflamed area, thereby reducing the inflammatory response. Despite its effectiveness, colchicine has side effects that may impact compliance with the medication regimen. These include gastrointestinal disturbances such as severe diarrhea, abdominal pain, nausea, and vomiting. Health care providers should discuss this drug thoroughly with the client so that gout can be adequately managed. See Table 6.15 for additional information on colchicine.

Allopurinol

Allopurinol is a medication used primarily to manage gout and certain other conditions associated with elevated levels of uric acid in the body. It is classified as a xanthine oxidase inhibitor and primarily works to lower uric acid levels in the body by inhibiting the enzyme xanthine oxidase.

When uric acid crystals accumulate in the joints, they can provoke an inflammatory response by activating the immune system. This leads to the release of inflammatory cytokines and other mediators that cause the characteristic swelling, redness, and pain associated with gout attacks. By lowering uric acid levels, allopurinol helps to reduce the frequency and severity of gout attacks, thereby indirectly contributing to the reduction of inflammation.

While allopurinol is effective in managing gout and preventing gout attacks, it may take several weeks or months of continuous use to achieve full benefits. See Table 6.14 for dosing information.

Probenecid

Probenecid is classified as a uricosuric agent, which means it works by increasing the excretion of uric acid in the urine. It does this by inhibiting the reabsorption of uric acid in the kidneys, which leads to more uric acid being eliminated from the body through urine. By increasing the excretion of uric acid, probenecid helps lower the levels of uric acid in the blood, reducing the risk of uric acid crystal formation and gout attacks. Probenecid indirectly helps to manage the inflammatory response associated with gout.

Table 6.14 lists common antigout drugs with typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Colchicine (Colcrys)	0.6 mg orally once or twice daily; maximum dose 1.2 mg per day.
Allopurinol (Zyloprim)	*For mild gout:* 200–300 mg/day orally. *For moderately severe tophaceous gout:* 400–600 mg/day orally.
Probenecid (Probalan)	250 mg orally twice daily for 2 weeks, followed by 500 mg orally twice daily thereafter.

TABLE 6.14 Drug Emphasis Table: Antigout Drugs (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects of antigout drugs include abdominal pain and cramping, nausea, vomiting, diarrhea, myopathy, abnormal liver and renal function, rash, and neuropathy. Common contraindications include hypersensitivity to the drug or any of its components, and renal or hepatic impairment.

Table 6.15 is a drug prototype table for antigout drugs featuring colchicine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antigout, alkaloid **Mechanism of Action** Inhibits expression of E-selectin on endothelial cells and prevents neutrophil adhesion	**Drug Dosage** 0.6 mg orally once or twice daily; maximum dose: 1.2 mg daily.
Indications Prophylaxis of gout flare-ups **Therapeutic Effects** Decreases inflammation and pain	**Drug Interactions** CYP3A4 inhibitors P-glycoprotein inhibitors HMG-CoA reductase inhibitors Fibrates Voriconazole Fluconazole Cimetidine Propafenone **Food Interactions** Grapefruit and grapefruit juice
Adverse Effects Gastrointestinal (abdominal cramps/pain, diarrhea, nausea/vomiting) Sensory motor neuropathy Rash Alopecia Leukopenia/thrombocytopenia/pancytopenia Elevated AST and/or ALT Myopathy and muscle weakness/pain Elevated CPK Azoospermia/oligospermia (conditions affecting sperm motility or sperm count)	**Contraindications** Hypersensitivity Renal impairment Hepatic impairment Caution: May cause colchicine toxicity when used concomitantly with CYP3A4 inhibitors and P-glycoprotein inhibitors

TABLE 6.15 **Drug Prototype Table: Colchicine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antigout drugs:

- Before administering antigout drugs, conduct a thorough assessment of the client's medical history, current medications, allergies, and kidney and liver function.
- Monitor the following laboratory studies: serum uric acid levels to assess effectiveness of medications in reducing uric acid levels, liver function for hepatotoxicity, renal function for nephrotoxicity, and electrolyte levels, which may be impacted by the use of these drugs.
- Educate the client about the drug's purpose, potential side effects, and benefits to help the client make an informed decision about the treatment plan.
- Some antigout drugs may have potential side effects or interactions with other medications. The nurse should be vigilant for signs of adverse effects and monitor for drug interactions that could affect the client's health.
- Antigout drugs, especially during initial treatment, may not provide immediate relief of symptoms during an acute gout attack. The nurse should offer emotional support and symptom management strategies to help alleviate pain and discomfort.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antigout drug should:

- Take the medication at the scheduled times and follow the prescribed dosage. Consistent adherence to the medication regimen helps control uric acid levels and prevent gout attacks.
- Maintain adequate hydration by drinking plenty of water throughout the day to help the kidneys flush out excess uric acid from the body.
- Report adverse effects such as rash, diarrhea, muscle pain, and weakness to the health care provider, as these may be adverse effects of the medication.
- Avoid purine-rich foods, such as red meats, organ meats, and seafood, as these can lead to increased uric acid levels in the body and exacerbate gout flare-ups.
- Keep follow-up appointments to have uric acid levels assessed and to ensure that medication management is effective.

The client taking an antigout drug *should not:*

- Become dehydrated when using probenecid, as this may increase the risk of kidney stone formation.
- Eat grapefruit or drink grapefruit juice when taking colchicine, as this may impact the efficacy of the drug.

Chapter Summary

This chapter provided a comprehensive understanding of the immune system and immunity, its significance in disease prevention, and the importance of vaccination. It explained the differences between natural and active acquired immunity as well as active and passive immunity. The chapter identified common diseases preventable through vaccination and emphasized the role of client education in promoting vaccine uptake for public health.

The chapter also introduced immunosuppressants, biologics, monoclonal antibodies, and biosimilar drugs, including their indications, actions, adverse reactions, contraindications, and potential interactions. Nursing implications for the safe administration and monitoring of these drugs, considering their impact on the immune system, were discussed.

The last section focused on understanding inflammation, its pathophysiology, and the five cardinal signs of inflammation. Causes and diagnostic studies related to inflammatory conditions were explored. The chapter covered the characteristics of drugs used to treat inflammation, their indications, mechanisms of action, potential adverse reactions, contraindications, and interactions. Nursing implications for the safe and effective administration of these drugs were emphasized, along with the importance of client education to promote adherence and effective management of these conditions.

Key Terms

active immunity the immune response generated by the body's own immune system after exposure to an antigen

adaptive immune system specific defense mechanism of the immune system that develops over time and provides a targeted response to pathogens or antigens

antibodies Y-shaped proteins produced by B cells of the immune system, also known as immunoglobulins

antibody-mediated/humoral immunity a type of immune response that primarily involves B cells and their production of antibodies

antigen-antibody interaction the binding of antigens (foreign substances) by specific antibodies produced by the immune system

biologic drugs medications derived from living organisms or produced using biotechnology

biosimilar drugs medications that are highly similar to an already approved biologic drug, known as the reference product

cell-mediated immunity type of immune response that primarily involves T cells in recognizing and responding to specific antigens

herd immunity the process by which a portion of a population becomes immune to a disease through either vaccination or previous infections

immune system a complex network of cells, tissues, and organs that work together to defend the body against infections, diseases, and foreign substances

immunizations the administration of vaccines to stimulate the body's immune system to produce a protective response against specific diseases

immunosuppressants medications that suppress or weaken the immune system's activity

infection when harmful microorganisms, such as bacteria, viruses, fungi, or parasites, invade the body and multiply, leading to disease

inflammation a natural response of the immune system to tissue injury, infection, or irritation

inflammatory response the coordinated reaction of the immune system to injury, infection, or harmful stimuli, involving a series of cellular and biochemical processes aimed at eliminating the threat and promoting tissue healing

innate immune system the body’s first line of defense against pathogens and foreign substances

monoclonal antibodies laboratory-produced molecules designed to mimic the immune system's natural ability to fight off specific pathogens or target specific cells

passive immunity the temporary protection against a specific pathogen that is conferred to an individual by receiving pre-formed antibodies rather than producing them internally

titer the concentration or potency of a substance, often an antibody, in a solution, indicating its effectiveness or level of activity

vaccine hesitancy the reluctance or refusal to receive vaccines despite their availability and effectiveness

vaccine-preventable diseases infectious diseases that can be effectively prevented by vaccination

vaccines biological preparations containing weakened or killed pathogens or antigens that stimulate the immune system to produce protective immunity against specific diseases

virulent the degree of severity or harmfulness exhibited by a pathogen, indicating its ability to cause severe disease or illness

Review Questions

1. A client is diagnosed with a viral infection. The health care provider prescribes antivirals to treat the infection. The nurse explains to the client that antivirals work by targeting the viral cells directly. Which type of immunity is primarily responsible for recognizing and attacking viral cells in this scenario?
    a. Innate immunity
    b. Passive immunity
    c. Antibody-mediated immunity
    d. Cell-mediated immunity

2. A client with rheumatoid arthritis (RA) is prescribed hydroxychloroquine as part of the treatment plan. The nurse is educating the client about the medication and its specific benefits for RA management. Which statement by the nurse best explains the application of hydroxychloroquine in treating RA?
    a. "Hydroxychloroquine works by directly suppressing the immune system, preventing it from attacking your joints and reducing RA symptoms."
    b. "Hydroxychloroquine acts as a pain reliever and anti-inflammatory medication, helping to alleviate joint pain and swelling associated with RA."
    c. "Hydroxychloroquine modifies the disease progression of RA by slowing down joint damage and preserving joint function over time."
    d. "Hydroxychloroquine enhances the production of specific antibodies that target the inflammation in your joints, leading to improved RA outcomes."

3. A client with rheumatoid arthritis is prescribed a biologic drug to manage the inflammatory condition. Before administering the biologic drug, which of the following is a priority for the nurse to assess to ensure the client's health and safety?
    a. Evaluate the client's tuberculosis (TB) status
    b. Measure the client's blood glucose level
    c. Check the client's vision and eye health
    d. Assess the client's vital signs

4. A client presents to the emergency department with a swollen, painful, and warm right ankle after a recent fall. The nurse observes redness and limited movement in the affected joint. The client's vital signs are stable. Based on the assessment findings, which conclusion should the nurse draw regarding the client's condition?
    a. The client is experiencing a localized allergic reaction, leading to inflammation and limited joint movement.
    b. The wound site shows signs of infection, indicated by the presence of redness, swelling, and warmth.
    c. The client is demonstrating the five cardinal signs of inflammation, suggesting the body's response to tissue injury.
    d. The wound may be due to poor blood circulation, causing localized redness and swelling.

5. A client is prescribed ibuprofen 800 mg every 6 hours for pain relief. On hand, there are ibuprofen tablets labeled 200 mg each. How many tablets should the nurse administer to the client for each dose?
    a. 2 tabs
    b. 3 tabs
    c. 4 tabs
    d. 5 tabs

6. A nursing student is studying about vaccines and immunizations. The student asks the instructor to clarify the difference between a vaccine and an immunization. How should the instructor respond?
    a. "A vaccine and an immunization are the same thing and can be used interchangeably to describe the process of protecting individuals from infectious diseases."
    b. "A vaccine is a preventive measure taken to minimize the risk of developing an infection, while an immunization is the body's natural ability to fight off diseases."

c. "A vaccine is a weakened or killed form of a disease-causing microorganism, while an immunization is the actual infection caused by the vaccine."
d. "A vaccine is a medication containing weakened or killed pathogens or antigens, given to prevent future infections, while an immunization is the process of administering the vaccine."

7. A client with osteoarthritis is prescribed indomethacin, a nonsteroidal anti-inflammatory drug (NSAID). The client has also been taking aspirin over the counter to assist with the pain. The nurse should monitor the client for which potential adverse effect?
a. Hyperglycemia
b. Respiratory depression
c. Gastrointestinal bleeding
d. Hypotension

8. A client with gout is prescribed an antigout drug to manage gout attacks. The nurse should advise the client to limit the daily intake of which food while on this medication?
a. Red meat
b. Dairy products
c. Fresh strawberries
d. Green, leafy vegetables

9. A client is planning to travel to a country with a high risk of hepatitis A infection. The health care provider recommends hepatitis A vaccination before the trip. The client asks the nurse about the difference between active and passive immunity. How should the nurse respond?
a. "Active immunity is a temporary form of protection acquired from the transfer of maternal antibodies during pregnancy. Passive immunity is achieved through vaccination, where your immune system responds to the vaccine and produces antibodies."
b. "Active immunity involves receiving pre-formed antibodies from an external source, like the hepatitis A vaccine. Passive immunity occurs when your immune system actively produces antibodies upon exposure to the live virus during an infection."
c. "Active immunity is achieved through receiving pre-formed antibodies from an external source, such as the hepatitis A vaccine. Passive immunity occurs when antibodies are passed from the birthing parent to the fetus/infant during pregnancy or when breastfeeding."
d. "Active immunity is conferred through the transfer of pre-formed antibodies from one person to another, such as receiving immune globulin for hepatitis A. Passive immunity is achieved through vaccination, which stimulates your immune system to produce antibodies."

10. A client with rheumatoid arthritis is prescribed adalimumab at a dose of 40 mg every other week. The vials of adalimumab available are labeled as 40 mg per 0.8 mL. How many milliliters should the nurse administer to the client for each dose?
a. 0.2 mL
b. 0.4 mL
c. 0.6 mL
d. 0.8 mL

CHAPTER 7
Anti-infective Drugs

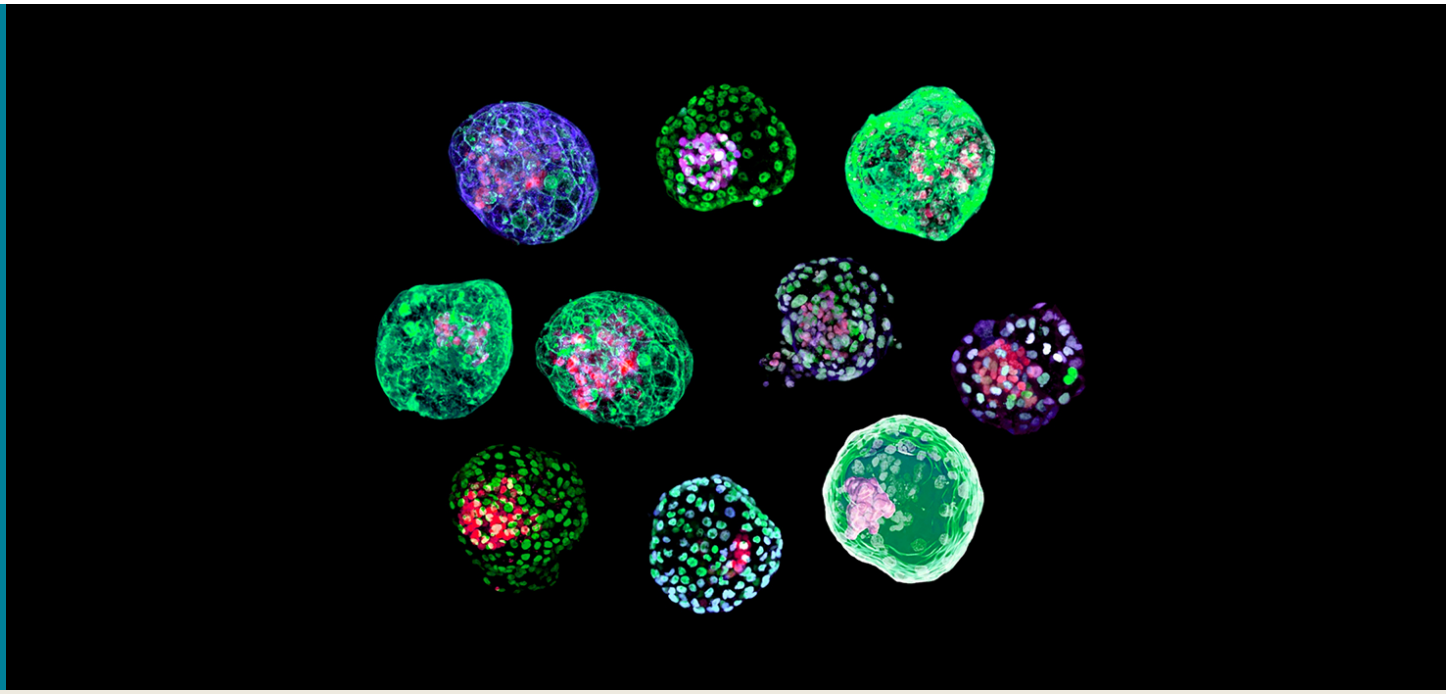


FIGURE 7.1 The immune system is a complex network of cells, tissues, and organs that work together to protect the body from harmful substances, such as pathogens. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Four primary types of microorganisms are responsible for causing infections in humans: bacteria, viruses, fungi, and parasites. This chapter will introduce the various pharmacologic agents designed to treat infections caused by these microorganisms, including indications, mechanisms, adverse effects, contraindications, and drug interactions.

7.1 Introduction to Bacterial, Viral/COVID-19, and Fungal Infections

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 7.1.1 Describe the pathophysiology of infection and the body's defense system.
- 7.1.2 Identify clinical manifestations related to infection.
- 7.1.3 Identify the etiology and diagnostic studies related to infection.

Infection and the Body's Defense System

The body's immune system has several different means of preventing infection from various microorganisms. These different barriers to infection can be broken down into two distinct types: innate immunity and adaptive immunity.

Innate immunity is the body's first line of defense against many types of organisms. It includes physical barriers

such as the skin, the acidic pH of the stomach, phagocytic cells (e.g., macrophages), and the inflammatory cascade (see Introduction to the Immune System and the Inflammatory Response). This type of immunity does not require prior exposure to an organism to provide protection and is not specific to any type of microorganism. Innate forms of immunity work quickly, within minutes to hours.

By comparison, **adaptive immunity**, also known as acquired immunity, is highly specific to individual microorganisms. Adaptive immunity works through various immune cells with the ability to recognize specific targets (antigens) as belonging to the self or as foreign. When the body detects foreign antigens, the adaptive immune system can mount a response against the pathogen to eliminate it (Figure 7.2). Adaptive immunity is initially slow upon the first exposure to an antigen, but it has a "memory" that allows it to mount fast responses upon repeated exposure to that same pathogen. This immune memory is durable and able to last the individual's whole life in some cases. This same process is how some vaccines work to induce immunity to organisms.

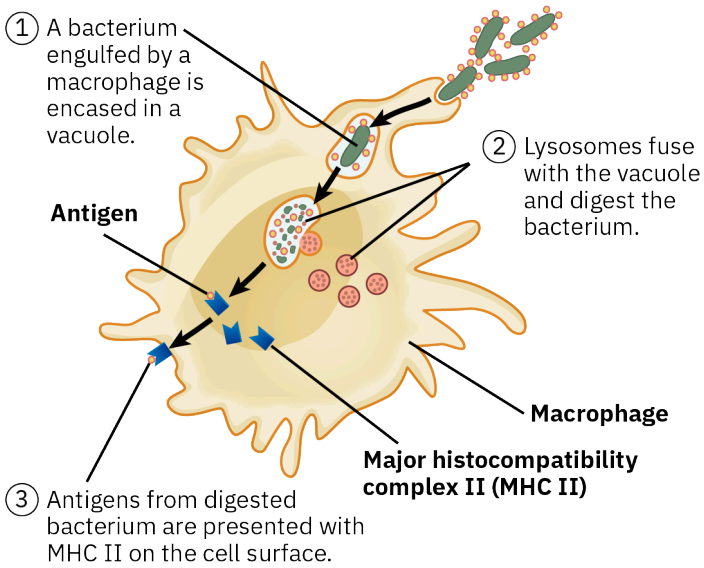


FIGURE 7.2 As part of the adaptive immune system, a macrophage engulfs and digests a foreign bacterium. (credit: modification of work from *Biology for AP® Courses*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

When microorganisms evade the innate and adaptive immunities, infection can occur. The individual may develop signs and symptoms consistent with elevated levels of inflammation that are caused by the immune system attempting to fight the infection. These signs and symptoms can include fever, malaise, nausea, vomiting, and pain.

Various diagnostic tests are available to aid in diagnosis of an infection. These include laboratory blood tests (e.g., a complete blood count can reveal white blood cell abnormalities), imaging (e.g., a chest x-ray can reveal pneumonia), and various direct and indirect organism tests (e.g., an influenza swab can reveal the presence of influenza viral antigens). The health care provider's choice of tests to order depends on the client.

People who are **immunocompromised** are more susceptible to, and have less immune defense against, infection. They may also be unable to mount "typical" signs and symptoms of infection, including fever, which can delay recognition of the infection. This can increase morbidity and mortality significantly in this client population because they are more prone to serious infections than clients with competent immune systems are. A client can be immunocompromised for a variety of reasons, such as by having human immunodeficiency virus (HIV) and the associated acquired immunodeficiency syndrome (AIDS), receiving chemotherapy for cancer treatment, or using corticosteroids (e.g., prednisone, dexamethasone). Nurses should take particular care to investigate any potential infections in clients who are immunocompromised.

Anti-infective Drugs

A variety of anti-infective medications are available today. Because many drugs are specific to the organisms that they treat, the first step in selection is to determine the most likely organism causing the infection. This allows for more judicious use of anti-infective medications and avoids the unnecessary use of drugs to treat organisms that are not present in the client. This consideration is commonly referred to as **anti-infective stewardship**.

Anti-infective drugs are grouped based on the organisms that they treat and include antibiotics, antivirals, antifungals, and antiparasitics. The following sections will detail the common types of anti-infectives, including their mechanisms of action, indications, adverse effects, and contraindications.

7.2 Antibiotic, Antiviral/Anti–COVID-19, and Antifungal Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 7.2.1 Identify the characteristics of drugs used to treat infection.
- 7.2.2 Discuss antibiotic drug resistance.
- 7.2.3 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat infection.
- 7.2.4 Describe the nursing implications of drugs used to treat infection.
- 7.2.5 Explain the client education related to drugs used to treat infection.

Antibiotics and Infection

Antibiotics are a group of drugs used specifically to treat infections caused by bacteria, either by directly killing the bacteria (**bactericidal**) or by suppressing their growth and multiplication (**bacteriostatic**). Antibiotics are some of the most commonly prescribed medications in the world; therefore, careful stewardship is necessary to avoid overuse, which can lead to antibiotic resistance.

Antibiotic Drug Resistance

Antibiotic drug resistance is the process by which bacteria become less responsive to antibiotics over time. As bacteria are exposed to antibiotics, evolutionary changes occur, leading to the development of resistant strains that can withstand the antibiotic exposure and continue to thrive. These changes can include modification of antibiotic targets (e.g., bacterial DNA or proteins) or the ability to remove a drug from the bacterial cell more effectively. Some bacteria are even able to share snippets of DNA that code for drug resistance with other bacteria.

Antibiotic resistance is a major public health issue. Having fewer options to treat a client's infection leads to worsened morbidity and mortality, higher health care costs, and the potential for bacteria to develop against which effective treatment does not exist. **Superinfections** can occur when the use of broad-spectrum antibiotics kills off normal nonpathogenic bacteria and leaves behind drug-resistant bacteria that can produce a new infection that is more difficult to treat (Figure 7.3). Most antibiotic drug resistance occurs due to antibiotic overuse, both in humans and in agriculture. This is why health care providers should prescribe antibiotics only when there is sufficient probability that the client has a bacterial infection.

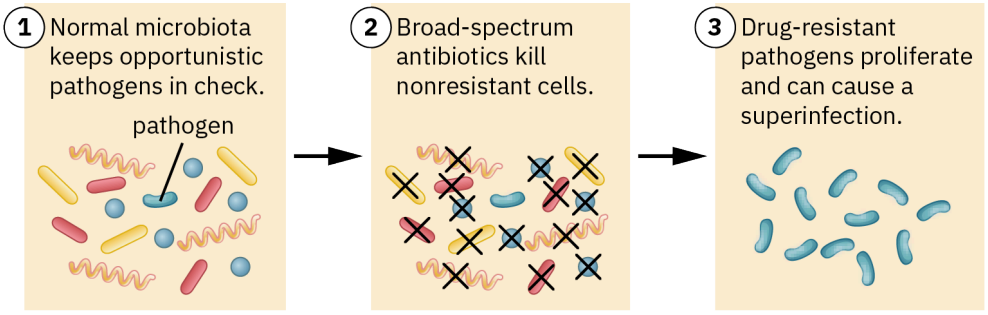


FIGURE 7.3 Broad-spectrum antibiotic use may lead to the development of a superinfection. (credit: modification of work from *Microbiology*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CLINICAL TIP

Antibiograms

Most hospital systems will develop a document known as an **antibiogram**. Cultured bacterial samples from clients at that hospital are used to determine regional bacterial resistance patterns against antibiotics. Antibiograms allow health care providers to make more informed decisions about which antibiotics are most effective in treating clients at their facility.

Antibiotic Drugs

The following sections cover the most common antibiotic agents available. Not every antibiotic is able to treat all types of bacteria equally, so health care providers must follow guidelines and antibiotic references to select the most appropriate antibiotic.

Penicillins

Penicillin, which was discovered in 1928 by Alexander Fleming, was the first antibiotic (American Chemical Society, n.d.). Since then, different drugs within the penicillin family have been developed, including nafcillin, piperacillin, and the aminopenicillins amoxicillin and ampicillin. These agents are used for a variety of infections, including streptococcal pharyngitis (strep throat), acute otitis media, and endocarditis.

Penicillins are part of the family of beta-lactam antibiotics because they include a beta-lactam ring in their chemical structure. The beta-lactam ring is critical for the antibiotic actions of penicillins. Penicillin-binding protein is a bacterial enzyme that is necessary to form the cross-links in the bacterial cell wall that provide structural integrity. When a penicillin is administered, the beta-lactam ring of penicillin will bind to the penicillin-binding protein and inhibit it. This inhibition causes fewer cross-links to form, thereby producing holes in the bacterial cell wall, leakage of internal contents, and cellular death of the bacteria.

Beta-Lactamase Inhibitors

One way that bacteria become resistant to antibiotics, such as penicillins, is by producing enzymes that can neutralize the drug. Beta-lactamase is one such enzyme; it is produced in resistant bacteria to cleave the beta-lactam ring found in drugs like penicillin to render it ineffective. Beta-lactamase inhibitors such as sulbactam, clavulanic acid, and tazobactam were produced to be administered with certain penicillins to help them retain and expand their activity to treat even more types of bacteria, such as anerobic organisms (e.g., *Peptostreptococcus* sp.). The most common combinations include amoxicillin plus clavulanic acid (Augmentin), ampicillin plus sulbactam (Unasyn), and piperacillin plus tazobactam (Zosyn).

Cephalosporins

Cephalosporins are another group of beta-lactam antibiotics and share the same mechanism of action as penicillin. The major differences between cephalosporins and penicillins are the various bacteria they have activity against and, thus, the types of infections they are best suited to treat.

Cephalosporins are divided into several different generations based on their spectrum of activity. First-generation cephalosporins include cephalexin and cefazolin; these are used for a variety of conditions such as uncomplicated urinary tract infections, upper respiratory tract infections, and prevention of infection during surgery. Second-generation cephalosporins, such as cefoxitin and cefprozil, are used for similar conditions, including otitis media, pneumonia, and urinary tract infections. Third-generation cephalosporins include ceftriaxone and cefotaxime. These agents have increased gram-negative bacterial coverage and are useful in the hospital setting for a variety of more serious infections, such as meningitis, pneumonia, and neonatal sepsis. The only fourth-generation cephalosporin currently available is cefepime. Cefepime has broad antimicrobial coverage, including the difficult-to-treat gram-negative organism *Pseudomonas aeruginosa*. Finally, the fifth-generation cephalosporin ceftaroline is relatively new and has the unique aspect of being the only cephalosporin to have activity against methicillin-resistant *Staphylococcus aureus* (MRSA), which is associated with significant morbidity and mortality.

Macrolides

Macrolide antibiotics include the agents azithromycin, clarithromycin, and erythromycin. These agents work by inhibiting protein production by the bacterial ribosomes. Macrolides and other protein synthesis inhibitors do not directly kill bacterial cells, but they sufficiently suppress their reproduction enough to allow the client's immune system to eliminate the bacteria. Macrolides treat infections caused by atypical bacteria that do not fall into the gram-positive or gram-negative categorization, including *Mycoplasma pneumoniae, Legionella pneumophila*, and *Chlamydia pneumoniae*. Therefore, macrolides are useful for treating a variety of respiratory conditions, such as pneumonia and Legionnaires' disease, as well as chlamydia, a sexually transmitted infection (STI).

Macrolides inhibit the liver enzyme cytochrome P450 3A4 (CYP3A4), which is responsible for metabolizing many medications. Medications that use the CYP enzyme system for metabolism will not undergo metabolism at the rate expected, leading to increased serum drug levels. This can result in adverse reactions and toxicity. Some examples

of drugs that would be affected include amlodipine, nifedipine, diltiazem, verapamil, lovastatin, simvastatin, carbamazepine, buspirone, midazolam, fluoxetine, sertraline, fluvoxamine, and dextromethorphan. (This is not an exhaustive list.)

Glycopeptides

The glycopeptide class of drugs includes vancomycin, a common antibiotic used in the hospital setting for treating infections caused by gram-positive bacteria, including MRSA. Vancomycin works by disrupting the integrity of the bacterial cell wall, leading to cellular death. Interestingly, oral vancomycin has good activity against *Clostridioides difficile*, which is an opportunistic pathogen that can cause colitis and severe diarrhea after clients receive antibiotics that disrupt the gut's normal bacterial flora. However, it is completely ineffective against bloodstream pathogens. Vancomycin is entirely renally eliminated and must be monitored by checking renal function and serum blood levels of the drug to ensure proper dosing.

Oxazolidinones

Oxazolidinones include the medication linezolid, which is commonly used to treat gram-positive infections that are highly resistant to agents such as vancomycin. One such infection is vancomycin-resistant *Staphylococcus aureus* (VRSA), which is difficult to treat. Oxazolidinones work by inhibiting bacterial protein synthesis to suppress further growth and multiplication of the bacteria.

Lincosamides

The lincosamide category is primarily represented by the drug clindamycin, a protein synthesis inhibitor. Clindamycin possesses strong gram-positive coverage (including against MRSA) and is also able to treat anaerobic bacterial infections. This allows clindamycin to be used in a variety of conditions, such as skin infections, animal bites, and topically as a treatment for acne.

Tetracyclines

The tetracyclines include the medications tetracycline, doxycycline, and minocycline. These work by inhibiting bacterial protein synthesis, which suppresses their growth. They possess good coverage against a wide variety of bacteria, making them ideal agents for treating conditions such as acne, Lyme disease, and anthrax.

Aminoglycosides

The aminoglycosides, including gentamicin, tobramycin, and amikacin, are used commonly in the hospital setting for their broad-spectrum gram-negative activity, including against infections caused by *Pseudomonas aeruginosa.* The aminoglycosides work by inhibiting bacterial protein synthesis. They are entirely renally eliminated, and renal function must be monitored along with serial serum drug levels to ensure that aminoglycosides do not accumulate in the body.

Fluoroquinolones

The fluoroquinolones include drugs such as ofloxacin, levofloxacin, ciprofloxacin, and moxifloxacin. These are commonly used to treat a variety of respiratory and urinary tract infections due to their excellent coverage of gram-negative, gram-positive, and atypical bacteria. Fluoroquinolones work by inhibiting the bacterial enzyme DNA gyrase. This enzyme is responsible for the winding and unwinding of bacterial DNA. Inhibition of this enzyme leads to increased DNA strand breakage, leading to eventual programmed cell death (**apoptosis**).

Sulfonamides

The sulfonamide category of antibiotics includes the combination product of sulfamethoxazole and trimethoprim (Bactrim). This combination has a broad spectrum of coverage, making it effective for treating urinary tract infections, infectious diarrhea, and skin infections. Sulfamethoxazole and trimethoprim work at different steps along the folic acid pathway necessary for the bacterial cell to produce nucleotides and, subsequently, DNA, RNA, and proteins; the drug combination's interference thus leads to cell death.

Nitroimidazoles

The nitroimidazoles include the drugs metronidazole and tinidazole. These agents are unique in the antibacterial category because they have good activity against anaerobic bacteria and protozoa, making this class useful for treating a number of STIs and vaginal infections. Nitroimidazoles work by entering the bacterial cell and disrupting the cell's DNA structure, leading to eventual cell death.

Table 7.1 lists common antibiotic drugs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Penicillin	
Benzathine penicillin G (Bicillin L-A)	*Streptococcal pharyngitis (strep throat):* *Adults:* 1.2 million units intramuscularly once. *Older children:* 0.9 million units intramuscularly once. *Children <60 lb:* 0.3–0.6 million units intramuscularly once.
Beta-Lactamase Inhibitor	
Amoxicillin-clavulanate (Augmentin)	*Otitis media:* *Adults:* 875 mg orally twice daily for 5–7 days. *Children:* 90 mg/kg/day orally, divided every 12 hours for 5–7 days.
Cephalosporin	
Cephalexin (Keflex)	*Skin or soft tissue infection:* *Adults and children ≥15 years:* 250 mg capsule orally every 6 hours or 500 mg orally every 12 hours for 7–14 days. For more severe infections, up to 4 g daily in 2–4 equally divided oral doses. *Children >1 year:* 25–50 mg/kg in equally divided oral doses for 7–14 days. For ß-hemolytic streptococcal infections, at least 10 days is recommended. In severe infections, a total daily dose of 50–100 mg/kg may be administered in equally divided oral doses.
Macrolide	
Azithromycin (Zithromax)	*Pneumonia, community acquired:* *Adults:* 500 mg orally on day 1, then 250 mg once daily for 4 days. *Children:* 10 mg/kg/dose orally on day 1, then 5 mg/kg/dose daily for 4 days.
Glycopeptide	
Vancomycin (Vancocin)	*Bloodstream infection:* Dosing is highly client dependent and requires drug serum monitoring for efficacy and safety. *Adults:* 2 g intravenously (IV) divided as either 500 mg every 6 hours or 1 g every 12 hours. Each dose should be administered over a period of at least 60 minutes. *Children:* 10 mg/kg/dose IV given every 6 hours. Each dose should be administered over a period of at least 60 minutes. C. difficile–*associated diarrhea:* *Adults:* 125 mg orally 4 times daily for 10 days. *Children:* 40 mg/kg in 3–4 divided oral doses for 7–10 days. Maximum daily dose: 2 g. *Staphylococcal enterocolitis:* *Adults:* 500–2000 mg orally in 3–4 divided doses for 7–10 days. *Children:* 40 mg/kg in 3–4 divided oral doses for 7–10 days. Maximum daily dose: 2 g.
Oxazolidinone	
Linezolid (Zyvox)	*Skin or soft tissue infection:* *Adults and children ≥12 years:* 600 mg orally or IV every 12 hours for 10–14 days. *Children <12 years of age:* 10 mg/kg IV or orally every 8 hours for 10–14 days.

TABLE 7.1 **Drug Emphasis Table: Antibiotics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Lincosamide	
Clindamycin (Cleocin)	*Osteomyelitis:* *Adults:* Orally: Serious infections: 150–300 mg every 6 hours. More severe infections: 300–450 mg every 6 hours. Intramuscularly or IV: 600–1200 mg/day in 2–4 equal doses. For more severe infections: 1200–2700 mg/day in 2–4 equal doses. *Children 1 month to 16 years:* Orally: Serious infections: 8–16 mg/kg/day in 3–4 equal doses. More severe infections: 16–20 mg/kg/day in 3–4 equal doses. Intramuscularly or IV: 20–40 mg/kg/day in 3–4 equal doses.
Tetracycline	
Doxycycline (Vibramycin)	*Rocky Mountain spotted fever:* *Adults and children ≥45 kg:* 200 mg orally on the first day of treatment (administered 100 mg every 12 hours) followed by a maintenance dose of 100 mg/day. For more severe infections, 100 mg every 12 hours. *Children <45 kg:* 2.2 mg/kg of body weight administered every 12 hours orally.
Aminoglycoside	
Gentamicin (Garamycin)	*Gram-negative infection:* Dosing is highly client dependent and requires drug serum monitoring for efficacy and safety. *Adults (intramuscular/IV):* 3 mg/kg/day in 3 equal doses administered at equal intervals. *Children (intramuscular/IV):* 6–7.5 mg/kg/day in 3 equal doses administered at equally divided intervals. Infusion should run 30–60 minutes.
Sulfonamide	
Sulfamethoxazole and trimethoprim (Bactrim)	*Urinary tract infection:* *Adults:* 1 double-strength tablet or 2 regular-strength tablets every 12 hours for 10–14 days. *Children ≥2 months:* 40 mg/kg sulfamethoxazole and 8 mg/kg trimethoprim per 24 hours, given in 2 doses every 12 hours for 10 days.

TABLE 7.1 **Drug Emphasis Table: Antibiotics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Most oral antibiotics can cause gastrointestinal discomfort, including nausea, vomiting, and diarrhea. A contraindication to any antibacterial is known hypersensitivity.

Allergic reactions, including anaphylaxis, are possible with penicillins. If a client has a severe allergy to any penicillin, then they should not receive any other drug in the penicillin class because they may experience a cross-sensitivity.

Most cephalosporins, except for ceftriaxone, must be renally dose adjusted to avoid adverse effects in clients with renal insufficiency. For many years there was concern that clients with a penicillin allergy could not receive cephalosporins due to risk for cross-reactivity and anaphylaxis. More recent data have shown that this concern is unfounded and that the largest risk is for clients with true anaphylactic reactions to penicillins receiving a first-generation cephalosporin. Later generations of cephalosporins carry a much lower risk and are safe to administer to clients with a history of penicillin allergy.

Macrolides are known to cause gastrointestinal discomfort because they activate motilin receptors in the intestines, which increases peristalsis, cramping, and diarrhea. Macrolides are also capable of inhibiting potassium efflux out of myocardial cells, leading to prolongation of the heart rate–corrected QT interval (QTc) on an electrocardiogram (ECG/EKG) and increasing the client's risk for developing torsades de pointes, a potentially fatal ventricular dysrhythmia.

Vancomycin is known to cause a severe flushing reaction when given too quickly intravenously, known as

vancomycin flushing syndrome. Vancomycin flushing syndrome can be mistaken for an allergic reaction, but all that is necessary to manage it is to slow the infusion of vancomycin and infuse it over at least 60 minutes. Elevated vancomycin levels are associated with risk for renal injury and hearing damage (ototoxicity). Older adults and those who are critically ill are especially at risk, so close monitoring of renal function and vancomycin blood levels is critical for successful use of the drug.

Unique adverse effects seen with tetracyclines include photosensitivity, skin discoloration, and risk for skeletal growth stunting and tooth discoloration. These last two effects occur because of the tetracyclines' ability to bind to calcium in developing bones and teeth. Recommendations to help prevent these effects include avoiding prolonged therapy (more than 21 days) in children who still have their baby teeth and avoiding use in pregnant clients during the second and third trimesters. Oral tetracyclines should not be taken with multivitamins or calcium-containing products. When taken together, tetracyclines will bind to metal ions such as iron and calcium, and the drug will not be absorbed; instead, it will be eliminated in the feces, leading to therapeutic failure.

Fluoroquinolones have a variety of safety issues, making screening for contraindications particularly important. In older adults and in clients with poor kidney function, fluoroquinolones are known to induce neuropsychiatric issues, including hallucinations and psychosis. Fluoroquinolones also increase the risk for tendonitis and tendon rupture. Fluoroquinolones can increase the QTc interval on ECG, which should be monitored for clients taking multiple QTc-prolonging medications and for those with congenital prolonged QTc to reduce risk for torsades de pointes. Fluoroquinolones should not be taken orally with multivitamins or calcium-containing products because this will cause the drug to bind to the metal and not be absorbed.

Table 7.2 is a drug prototype table for antibiotics featuring amoxicillin. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Aminopenicillin **Mechanism of Action** Inhibits bacterial cell wall synthesis, leading to bacterial cell lysis	**Drug Dosage** *Adults:* 500 mg orally every 12 hours. *Children:* 80–90 mg/kg/day orally divided every 12 hours.
Indications Treatment of infections due to susceptible organisms (*only* beta-lactamase-negative) **Therapeutic Effects** Treats infections caused by susceptible organisms	**Drug Interactions** Aminoglycosides Methotrexate Tetracyclines Probenecid Mycophenolate **Food Interactions** No significant interactions
Adverse Effects Nausea Vomiting Diarrhea Hypersensitivity Crystalluria Anemia Thrombocytopenia	**Contraindications** Hypersensitivity Caution: Renal impairment

TABLE 7.2 **Drug Prototype Table: Amoxicillin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antibiotics:

- Monitor for signs and symptoms of anaphylaxis (e.g., shortness of breath, difficulty breathing, difficulty swallowing).

- Advise the client to take the entire prescribed course of the medication to ensure adequate treatment and to reduce the development of antibiotic drug resistance.
- Instruct the client to maintain adequate hydration; monitor kidney function for renally eliminated medications, such as penicillins, most cephalosporins, vancomycin, aminoglycosides, and particularly fluoroquinolones.
- For clients taking macrolides, always review their medication list for medications metabolized by CYP3A4.
- Monitor for thrombocytopenia, leukopenia, and anemia in clients receiving linezolid. Monitor complete blood count (CBC) periodically. Notify prescriber if blood counts drop.
- If client is taking any medication that can increase serotonin levels (SSRIs, SNRIs, or MAOIs), the nurse should observe for signs of serotonin syndrome, including hyperthermia, headache, confusion, agitation, increased blood pressure, tachycardia, tremor, ataxia, muscle rigidity, and seizures.
- Ensure that any ordered samples for serum levels of agents such as vancomycin and aminoglycosides are obtained at the intended time so that accurate dosage adjustments can be made. Timing may include peak levels drawn after a dose of the antibiotic has been given or trough levels drawn immediately before a dose.
- Monitor for severe or bloody diarrhea and, if ordered, obtain a sample to check for *C. difficile*.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antibiotic should:

- Alert their health care provider about any signs and symptoms of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider about any recent antibiotic use prior to starting therapy.
- Alert their health care provider that they are taking antibiotics, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take the entire course of antibiotics, even if they begin to feel better.
- Take a missed dose as soon as they remember; however, they should *not* take double doses.

The client taking an antibiotic *should not:*

- Take multivitamins or calcium-containing products with fluroquinolone or tetracycline drugs.

FDA BLACK BOX WARNING

Antibacterials

All antibacterials: *Clostridioides difficile*–associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including clindamycin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon, leading to overgrowth of *C. difficile*.

Aminoglycosides can cause neurotoxicity, manifested by ototoxicity, both vestibular and auditory. This can occur in clients treated with gentamicin, primarily in those with preexisting renal damage and in clients with healthy renal function treated with higher doses and/or for longer periods than recommended. Aminoglycoside-induced ototoxicity is usually irreversible. Other manifestations of neurotoxicity may include numbness, skin tingling, muscle twitching, and convulsions. Monitor serum concentrations of aminoglycosides when feasible to ensure adequate levels and to avoid potentially toxic levels.

Fluoroquinolones have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together, including tendinopathy and tendon rupture, peripheral neuropathy, and central nervous system effects. Discontinue ciprofloxacin immediately and avoid the use of fluoroquinolones in clients who experience any of these serious adverse reactions. Because fluoroquinolones have been associated with serious adverse reactions, ciprofloxacin is reserved for use in clients who have no alternative treatment options for the following indications: acute exacerbation of chronic bronchitis, acute sinusitis, and acute uncomplicated cystitis.

Fluoroquinolones also may exacerbate muscle weakness in clients with myasthenia gravis. Avoid ciprofloxacin in clients with known history of myasthenia gravis.

Vancomycin: A formulation of this injection contains the excipients polyethylene glycol (PEG 400) and N-acetyl D-alanine (NADA), which resulted in fetal malformations in animal reproduction studies at dose exposures approximately 8 and 32 times, respectively, higher than the exposures at the human equivalent dose. If use of vancomycin is needed during the first or second trimester of pregnancy, use other available formulations of vancomycin.

Viruses and Antiviral Drugs

Compared to bacteria, viruses are simple microorganisms made up of single or double strands of DNA or RNA inside a cellular coating known as a capsid. Viruses are unique in that they are unable to replicate on their own. Instead, a virus will harness the host's cellular mechanisms to make new copies of itself to then infect other cells. Most viral infections (e.g., adenoviruses, rhinoviruses) are minor and self-limited, meaning they rarely require drug therapy. More serious viral infections, including those caused by the hepatitis viruses, pose much more significant risks to clients and require specific antiviral therapy. Clients at risk for more serious viral infections include individuals at the extremes of age (i.e., the very young and the very old) and those who are immunocompromised.

The following section covers the common antiviral drugs used to treat a variety of viral infections, including those caused by hepatitis, herpes, and influenza viruses. The mechanisms of action, drug interactions, adverse effects, and indications are discussed, including special considerations for use.

Hepatitis Antivirals

Hepatitis viruses are clinically important because they can cause inflammation and damage to the liver. The three main types are hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV). HAV infection is usually self-limited, with many individuals being able to rid themselves of it without any intervention. HBV and HCV infections are of more clinical concern because without intervention, many clients will develop chronic infection, which can lead to cirrhosis, liver failure, and risk for liver cancer. HAV is spread via the fecal–oral route, and HBV and HCV are usually spread through parenteral transmission (such as by sharing contaminated needles) and during sexual intercourse. Vaccines can prevent HAV and HBV infections.

Medications to treat chronic HBV infection are not always curative and are used with the goal of preventing complications such as cirrhosis and liver cancer. HBV infection is typically managed with nucleoside/nucleotide antivirals, which include entecavir, tenofovir, lamivudine, adefovir, and telbivudine. These drugs work against viral DNA polymerase, an enzyme critical for DNA production and viral replication. They are incorporated into the viral DNA and function as "chain terminators," meaning that no other nucleotides may be added onto them in the chain of DNA, and DNA production is thereby halted. Another treatment option is interferon (interferon alfa); however, due to toxicity, this medication is considered a last resort when all else fails.

HCV infection previously was a chronic disease with no definitive cure and consisted of treatment with parenteral medications with poor tolerability (e.g., interferons). This condition has radically changed, and now many clients with HCV can achieve **virologic cure** (no presence of the virus in the body) with 12–24 weeks of oral drug therapy using a direct-acting antiviral (DAA) agent such as sofosbuvir. The DAAs can work on a variety of steps in the HCV life cycle to prevent replication or transmission of active virus. Nurses should stress to clients that they must take the entire course of their DAA regimen because resistance can develop if the virus is not completely suppressed. More resistant cases may require treatment with the injectable drug ribavirin, the action of which is not currently understood.

Herpes Antivirals

Two main types of herpes viruses are responsible for causing clinically significant disease. Herpes simplex virus (HSV)-1 is usually responsible for causing lesions (e.g., cold sores) on the mouth, face, and skin. HSV-2 is usually responsible for infections in the genitals and rectum. No curative therapy for HSV-1 or HSV-2 currently exists, but medication is useful to reduce the duration and severity of symptoms a client experiences and to help prevent spread of the virus to other individuals. Agents used to treat herpes viruses include acyclovir and its oral prodrug, valacyclovir, as well as famciclovir. Ganciclovir, valganciclovir, and cidofovir also have activity against herpes viruses,

but due to multiple adverse effects, they are reserved for cases of resistance to the first-line agents. These agents work by inhibiting the formation of new viral DNA by acting as chain terminators.

Clients with herpes virus infections may take these medications either when symptoms occur (episodic therapy) or every day for chronic suppression. Chronic suppression is linked to lower incidence of transmission of the virus to uninfected individuals and is useful for clients who have multiple outbreaks each year. Clients using the episodic method must be instructed to begin taking their therapy within 24 hours of symptom onset for the medication to be effective. They should also be informed that viral shedding can occur even without an active lesion, which may increase transmission risk.

Influenza Antivirals

Influenza refers to a diverse set of viruses known to cause upper respiratory tract illnesses, most commonly in the winter months. Annual vaccination will not prevent all infections but may help reduce the symptoms that individuals experience, and it is critical for protecting people most at risk for complications, such as older adults and immunocompromised individuals. However, vaccines are able to protect against only four strains each year with the current quadrivalent vaccines, which protect against two strains of influenza A and two of influenza B. This means that many people still go on to develop influenza infections that require treatment with medications.

The primary class of drugs used to treat influenza infection includes the neuraminidase inhibitors oseltamivir, zanamivir, and peramivir. Neuraminidase inhibitors work by inhibiting the enzyme neuraminidase, which is used to cleave mature copies of the virus from an infected cell to allow it to go infect other cells. Inhibiting this enzyme prohibits the virus from infecting host cells. If the client has had flulike symptoms for more than 48 hours, neuraminidase inhibitors should not be used due to lack of efficacy.

Oseltamivir is considered the first-line option for treatment of influenza and is given orally over 5 days. Zanamivir is an inhaled neuraminidase inhibitor that can be used as an alternative to oral oseltamivir. Peramivir is the only intravenous neuraminidase inhibitor and should be reserved for clients who cannot take oral or inhaled medications.

Table 7.3 lists common antivirals and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Acyclovir (Zovirax)	*Herpes simplex virus, mucocutaneous infection:* *Adults:* *Oral:* 400 mg 3 times daily for 7–10 days. *IV:* 10 mg/kg/dose every 8 hours for 7 days. *Children:* *Oral:* 40–80 mg/kg/day divided into 3–4 doses per day for 7–10 days; maximum dose: 1200 mg/day. *IV:* 5 mg/kg/dose every 8 hours for 7 days.
Oseltamivir (Tamiflu)	*Influenza:* 75 mg orally twice daily for 5 days.
Sofosbuvir (Sovaldi)	*Chronic hepatitis C virus infection:* 400 mg orally once daily for 16 weeks.
Tenofovir (Viread)	*Hepatitis B virus infection:* 300 mg orally once daily for 28 days.

TABLE 7.3 **Drug Emphasis Table: Antivirals** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Antiviral agents are known to cause gastrointestinal discomfort, including nausea, vomiting, and diarrhea. A contraindication to any antiviral drug is known hypersensitivity.

The nucleoside/nucleotide analogs used to treat HBV infection are considered safer than interferon products, but individual agents may be linked to serious complications such as entecavir-induced lactic acidosis and adefovir-induced nephrotoxicity.

Side effects of herpes antivirals are mild but can include blood cell production suppression, malaise, and risk for

renal injury.

Zanamivir is given via inhalation and should not be used in clients with a history of asthma or chronic obstructive pulmonary disease due to risk for bronchospasm (tightening of the airways).

Table 7.4 is a drug prototype table for antivirals featuring acyclovir. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antiviral agent **Mechanism of Action** Inhibits DNA synthesis and viral replication by competing with deoxyguanosine triphosphate for viral DNA polymerase and being incorporated into viral DNA	**Drug Dosage** *Herpes simplex virus, mucocutaneous infection:* *Adults:* *Oral:* 400 mg 3 times daily for 7–10 days. *IV:* 10 mg/kg/dose every 8 hours for 7 days. *Children:* *Oral:* 40–80 mg/kg/day divided into 3–4 doses per day for 7–10 days; maximum dose: 1200 mg/day. *IV:* 5 mg/kg/dose every 8 hours for 7 days.
Indications Treatment of infections due to susceptible viruses (e.g., herpes simplex virus, cytomegalovirus) **Therapeutic Effects** Treats viral infections caused by susceptible organisms	**Drug Interactions** Clozapine Theophylline Tizanidine Zidovudine **Food Interactions** No significant interactions
Adverse Effects Nausea Vomiting Diarrhea Hypersensitivity Crystalluria Malaise Increased serum creatinine/acute kidney injury	**Contraindications** Hypersensitivity Caution: Intravenous injection extravasation Renal impairment

TABLE 7.4 **Drug Prototype Table: Acyclovir** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antivirals:

- Monitor for signs and symptoms of anaphylaxis (e.g., shortness of breath, difficulty breathing, difficulty swallowing).
- Advise the client to take the entire prescribed course of the medication to ensure adequate treatment and to reduce the development of drug resistance.
- Instruct the client to maintain adequate hydration; monitor kidney function for renally eliminated antivirals such as acyclovir and valacyclovir.
- Monitor the client's complete blood count to check for bone marrow suppression.
- Monitor for mental status changes in clients receiving intravenous antivirals who have poor renal function.
- For clients using antiviral medication episodically, teach them to begin taking it as soon as possible after symptom onset.
- Use appropriate personal protective equipment (e.g., mask and gloves) when clients are diagnosed with influenza to prevent infection spread.
- Check a pregnancy test in clients capable of pregnancy prior to initiating antiviral therapy.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antiviral should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider about any recent antiviral use prior to starting therapy.
- Alert their health care provider that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should *not* take double doses.
- For episodic use, begin taking the antiviral as soon as possible (within 24 hours of symptom onset) to reduce symptom duration.
- Stay well hydrated while using these medications to avoid kidney issues.

FDA BLACK BOX WARNING

Antivirals

Ganciclovir: Granulocytopenia, anemia, thrombocytopenia, and pancytopenia have been reported with ganciclovir.

Ganciclovir: Based on animal data and limited human data, ganciclovir may cause temporary or permanent inhibition of spermatogenesis in males and suppression of fertility in females, may cause birth defects in humans, and has the potential to cause cancer in humans.

Cidofovir: Renal impairment is the major toxicity of cidofovir. Cases of acute renal failure resulting in dialysis and/or contributing to death have occurred with as few as one or two doses of cidofovir. Cidofovir is contraindicated in clients who are receiving other nephrotoxic agents.

Sofosbuvir: HBV reactivation has been reported in HCV/HBV coinfected clients who were treated with HCV antivirals but were not receiving HBV antiviral therapy.

Tenofovir: Acute exacerbations of HBV have been reported in clients who have discontinued HBV antiviral therapy.

COVID-19 and Anti–COVID-19 Drugs

In 2020, the coronavirus disease 2019 (COVID-19) caused by the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) led to a global pandemic that resulted in millions of deaths (World Health Organization, n.d.). Given the severity of illness and the propensity of the virus to kill individuals with poor immune systems and multiple comorbidities, there was a rush to develop both vaccines against the virus and medications to treat individuals with COVID-19 infections.

This section focuses on drug therapy for clients with an existing COVID-19 infection. It is important to note that treatment for COVID-19 is still an evolving topic and more research is still being conducted, so health care professionals should always consult the Centers for Disease Control and Prevention (CDC) COVID-19 website (https://openstax.org/r/coronavirus) for up-to-date guidance.

Note that COVID-19 can present as asymptomatic or with potentially life-threatening symptoms. The variation can be due to issues such as vaccination status, medical comorbidities, immune system status, and age. These factors should always be considered when deciding whether COVID-19 drug therapy is needed. Clients without risk factors for progression to severe disease and those who are asymptomatic can be managed with supportive care and without drug treatment.

Nirmatrelvir

Nirmatrelvir is an oral antiviral medication that works by inhibiting the protease enzyme that is necessary to develop

mature proteins. Because these proteins are prevented from being made, new mature virus copies cannot be made. Nirmatrelvir is combined with ritonavir, which is used as a strong CYP3A4 inhibitor to boost levels of nirmatrelvir and reduce dosing frequency. Because ritonavir is combined with nirmatrelvir, the nurse must review a client's medication profile to avoid any significant CYP3A4 interactions. Nirmatrelvir should be taken as soon as possible once symptoms occur because it loses efficacy and is not recommended after 5 days of symptom onset.

Remdesivir

Remdesivir works by inhibiting viral RNA polymerase, causing inhibition of viral protein synthesis and reproduction. Remdesivir is an intravenous product, so it is usually reserved for hospitalized clients or those who cannot receive nirmatrelvir within 7 days of symptom onset.

Molnupiravir

Molnupiravir is an oral product that works by being incorporated into the SARS-CoV-2 RNA; it then induces errors that lead to inhibited viral reproduction. There are some questions about the efficacy of molnupiravir in the treatment of COVID-19, so it is recommended as an alternative if clients cannot receive nirmatrelvir due to drug interactions or impaired renal function. Initiation of molnupiravir should occur within 5 days of symptom onset.

Table 7.5 lists anti–COVID-19 drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Molnupiravir (Lagevrio)	800 mg orally every 12 hours for 5 days.
Nirmatrelvir/ritonavir (Paxlovid)	300 mg nirmatrelvir plus 100 mg ritonavir orally twice daily for 5 days.
Remdesivir (Veklury)	200 mg IV once on day 1, then 100 mg IV once daily for 4 days.

TABLE 7.5 Drug Emphasis Table: Anti–COVID-19 Drugs (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Anti–COVID-19 drugs are known to cause gastrointestinal discomfort, including nausea, vomiting, and diarrhea. A contraindication to any antiviral drug is known hypersensitivity.

Nirmatrelvir is well tolerated, with diarrhea and dysgeusia (impaired sense of taste) being the most frequently reported adverse effects. Adverse effects seen with the use of remdesivir include elevated serum glucose levels and reduced kidney function. Remdesivir should be administered only when emergency airway tools (e.g., laryngoscope) are available in case of a severe allergic reaction.

Table 7.6 is a drug prototype table for anti–COVID-19 drugs featuring nirmatrelvir/ritonavir. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antiviral agent **Mechanism of Action** Inhibits the SARS-CoV-2 main protease, which inhibits viral replication	**Drug Dosage** 300 mg nirmatrelvir plus 100 mg ritonavir orally twice daily for 5 days.
Indications COVID-19 infection **Therapeutic Effects** Treats infections caused by the SARS-CoV-2 virus	**Drug Interactions** CYP3A4 substrates Alprazolam Buprenorphine Cabotegravir **Food Interactions** No significant interactions
Adverse Effects Diarrhea Dysgeusia Bradycardia Pruritus	**Contraindications** Hypersensitivity Caution: Liver impairment

TABLE 7.6 **Drug Prototype Table: Nirmatrelvir/Ritonavir** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking anti–COVID-19 drugs:

- Monitor for signs and symptoms of anaphylaxis (e.g., shortness of breath, difficulty breathing, difficulty swallowing).
- Advise the client to take the entire prescribed course of the medication to ensure adequate treatment and to reduce the development of drug resistance.
- Monitor clients taking remdesivir for elevated serum glucose levels and renal function abnormalities.
- Monitor clients receiving nirmatrelvir/ritonavir for hepatic dysfunction.
- Advise the client to begin taking medications as soon as possible after symptom onset to ensure efficacy.
- Review the client's medication list prior to initiating ritonavir to evaluate for CYP3A4 interactions.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an anti–COVID-19 drug should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should *not* take double doses.

Fungi and Antifungal Drugs

Fungi make up a diverse group of microorganisms that includes yeasts, molds, and mushrooms. Some of the key differences between human and fungal cell structures are that fungi introduce sterols into the cell membrane, and they have a cell wall that includes products such as chitin and glucans. These differences form the basis for drug therapy designed to eliminate fungi. Fungal infections can vary in presentation from less severe infections of the scalp, skin, or nails, which may require topical antifungal therapy, to severe systemic fungal infections that may be life-threatening. The latter are primarily found in immunocompromised clients and require aggressive systemic therapy to avoid serious morbidity and mortality.

This section will cover commonly used antifungal drugs, including their mechanisms of action, adverse effects, indications, and contraindications. Given the wide variety of fungi that can cause disease (e.g., *Aspergillus*, *Candida*, *Blastomyces*), positive identification is ideal to ensure that the appropriate drug is selected. Unfortunately, fungal cultures can take weeks for identification. In severely ill clients, broad-spectrum antifungals are used until culture results are available.

Polyenes

Polyene antifungal drugs include amphotericin B and nystatin. These are broad-spectrum antifungals that bind to ergosterol in the fungal cell membrane, leading to membrane breakdown and fungal cell death. Amphotericin B is used intravenously to treat severe systemic fungal infections. Nystatin is used orally for infections such as oropharyngeal candidiasis (thrush). Nystatin is not absorbed systemically when taken orally or topically; therefore, it is ineffective for systemic infections.

Azoles

The azole antifungals include two broad classes: imidazoles and triazoles. Examples of imidazoles include clotrimazole, miconazole, and ketoconazole. Examples of triazoles include fluconazole, voriconazole, and posaconazole. These drugs work by inhibiting the enzyme 14-alpha-sterol demethylase. This enzyme is necessary for the fungal cell to produce ergosterol, which is then transferred to the cell membrane. Inhibition of this enzyme leads to arrest of fungal cell growth.

Antimetabolites

Flucytosine is the only antifungal antimetabolite. It works by being converted to 5-fluorouracil (5-FU) in the fungal cell; 5-FU inhibits the enzyme thymidylate synthase as well as DNA, RNA, and protein production in fungal cells, leading to arrested growth.

Echinocandins

The echinocandins include the drugs caspofungin, anidulafungin, and micafungin. These work by inhibiting the enzyme 1,3-beta-glucan synthase, which is responsible for providing structural integrity to the fungal cell wall. Inhibiting this enzyme decreases glucan synthesis and disrupts the cell wall, leading to fungal cell death.

Table 7.7 lists antifungal drugs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Amphotericin B (Fungizone)	*Progessive, potentially life-threatening fungal infections:* *Adults:* 0.25–0.3 mg/kg IV daily over 2–6 hours. Total daily dose of 1.5 mg/kg should not be exceeded.
Anidulafungin (Eraxis)	*Candida:* *Adults:* 200 mg IV on day 1, then 100 mg IV once daily. *Children:* 3 mg/kg (not to exceed 200 mg) on day 1, followed by a once daily IV maintenance dose of 1.5 mg/kg (not to exceed 100 mg) thereafter for 14 days. *Esophageal candidiasis:* *Adults:* 100 mg IV loading dose on day 1, followed by a 50 mg IV once daily maintenance dose for 14 days.
Fluconazole (Diflucan)	*Oropharyngeal or esophageal candidiasis:* *Adults:* 200 mg orally on the first day, followed by 100 mg orally once daily for 2 weeks to prevent relapse.
Flucytosine (Ancoban)	*Symptomatic cystitis:* *Adults:* 50–150 mg/kg/day administered in divided doses at 6-hour intervals for 10 days.
Nystatin (Nystat)	*Oropharyngeal candidiasis:* *Adults and children:* Swish and swallow 400,000–600,000 units 4 times daily for 7–14 days. Continue for 48 hours after symptoms resolve and a negative culture is obtained. *Infants:* 200,000 units 4 times daily using a dropper.

TABLE 7.7 **Drug Emphasis Table: Antifungal Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Antifungals are known to cause gastrointestinal discomfort, including nausea, vomiting, and diarrhea. A contraindication to any antifungal drug is known hypersensitivity.

Amphotericin B is very toxic and can cause flulike symptoms during infusion, hypotension, renal toxicity, and electrolyte disturbances. To reduce these adverse effects, several formulations have been developed that incorporate the drug into a lipid membrane. This significantly increases medication costs but is much better in reducing client harm.

SAFETY ALERT

Oral/Intravenous Azole Antifungals

Some oral and intravenously administered azole antifungals are strong inhibitors of CYP3A4, which can affect many medications. Affected medications will have higher levels in the body and increase the risk for drug toxicity. The health care provider should screen a client's medication profile for interactions before initiating therapy with an oral or intravenous azole antifungal.

Table 7.8 is a drug prototype table for antifungal drugs featuring fluconazole. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Azole antifungal **Mechanism of Action** Inhibits fungal cytochrome P450 activity, decreasing ergosterol synthesis and inhibiting cell membrane formation	**Drug Dosage** *Oropharyngeal or esophageal candidiasis:* *Adults:* 200 mg orally on the first day, followed by 100 mg orally once daily for 2 weeks to prevent relapse.
Indications Treatment of fungal infections caused by susceptible fungi **Therapeutic Effects** Treats fungal infections caused by susceptible organisms	**Drug Interactions** CYP3A4 substrates Amiodarone Carvedilol Diazepam **Food Interactions** No significant interactions
Adverse Effects Headache Skin rash Abdominal pain Diarrhea Dizziness QT interval prolongation	**Contraindications** Hypersensitivity Pregnancy Coadministration with QT interval–prolonging drugs Caution: Central nervous system impairment Renal impairment

TABLE 7.8 **Drug Prototype Table: Fluconazole** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antifungal drugs:

- Monitor for signs and symptoms of anaphylaxis (e.g., shortness of breath, difficulty breathing, difficulty swallowing).
- Advise the client to take the entire prescribed course of the drug to ensure adequate treatment and to reduce the development of drug resistance.
- Instruct the client to maintain adequate hydration; monitor kidney function with renally eliminated

medications.
- Ensure that blood samples for any drug levels ordered are obtained at the intended time in order to allow accurate assessments regarding dosage adjustments.
- Monitor the ECG for prolongation of the QTc interval when clients are taking systemically acting agents.
- Monitor liver function tests to assess for liver injury.
- Check a client's medication list prior to administering a systemic azole antifungal because oral and intravenous azole antifungals inhibit CYP3A4 and can cause many drug interactions.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antifungal should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider about any recent antifungal medication use prior to starting therapy.
- Alert their health care provider that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should *not* take double doses.
- Alert their health care provider about starting any new medications that may interact with their antifungal therapy.

FDA BLACK BOX WARNING

Amphotericin B

Amphotericin B should be used primarily for treatment of clients with progressive and potentially life-threatening fungal infections; it should not be used to treat noninvasive forms of fungal disease such as oral thrush, vaginal candidiasis, and esophageal candidiasis in clients with normal neutrophil counts.

7.3 Introduction to HIV, AIDS, and Antiretrovirals

LEARNING OUTCOMES

By the end of this section, you should be able to:
- 7.3.1 Describe the pathophysiology of HIV and AIDS.
- 7.3.2 Identify clinical manifestations related to HIV and AIDS.
- 7.3.3 Identify common risk factors for HIV transmission.
- 7.3.4 Identify etiology and diagnostic studies related to HIV and AIDS.
- 7.3.5 Identify characteristics of drugs used to treat HIV and AIDS.
- 7.3.6 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat HIV and AIDS.
- 7.3.7 Describe the nursing implications of drugs used to treat HIV and AIDS.
- 7.3.8 Explain the client education related to drugs used to treat HIV and AIDS.

Pathophysiology

The **human immunodeficiency virus** (HIV) is responsible for causing deterioration in the infected individual's immune system, leaving them vulnerable to a variety of opportunistic infections and cancers. This state of immunodeficiency is known as **acquired immunodeficiency syndrome (AIDS)**. Since HIV was first identified in the 1980s, highly effective medications for **antiretroviral therapy (ART)** have been developed to suppress the virus and delay the development of AIDS-defining illnesses such as *Pneumocystis jirovecii* pneumonia (PJP; previously known as *Pneumocystis carinii* pneumonia or PCP), cytomegalovirus (CMV) infection, and the cancer known as Kaposi's sarcoma. However, HIV infection is a lifelong condition with no known curative treatment.

After the individual's initial exposure to HIV, the virus targets the CD4 T lymphocytes (helper T cells). It binds to and fuses with the CD4 cell and then enters it. From there, the enzyme reverse transcriptase takes the HIV RNA and forms a complementary strand of DNA. The enzyme integrase then incorporates the viral DNA into the individual's DNA, which causes the host cell to begin producing viral proteins. The enzyme protease then cuts the viral proteins into their mature form, and the new copy of the virus is ready to bud off from the infected cell to go infect a new CD4 cell (Figure 7.4). As this process continues, there is continual degradation in the number of CD4 cells available to fight infection, and the person becomes immunocompromised and more at risk for various opportunistic infections and cancers. Once an individual develops one of these opportunistic illnesses or their CD4 cell count drops <200 cells/mL of blood, they are considered to have AIDS. People with AIDS have badly damaged immune systems. Understanding the life cycle of the virus is important because these steps present different drug targets that can be used to suppress viral replication. HIV treatment can slow or prevent progression of the disease. There are three stages of HIV. The first stage is acute HIV infection, in which clients have a large amount of HIV in their blood and are very contagious. Many have flu-like symptoms. Stage two is chronic HIV infection, also called asymptomatic HIV infection or clinical latency. HIV is still active, and the client can still transmit the infection to others as it continues to reproduce in the body. The third stage is when the client is diagnosed with AIDS. This is the most severe form of HIV. Clients have a high viral load and can easily transmit the virus.

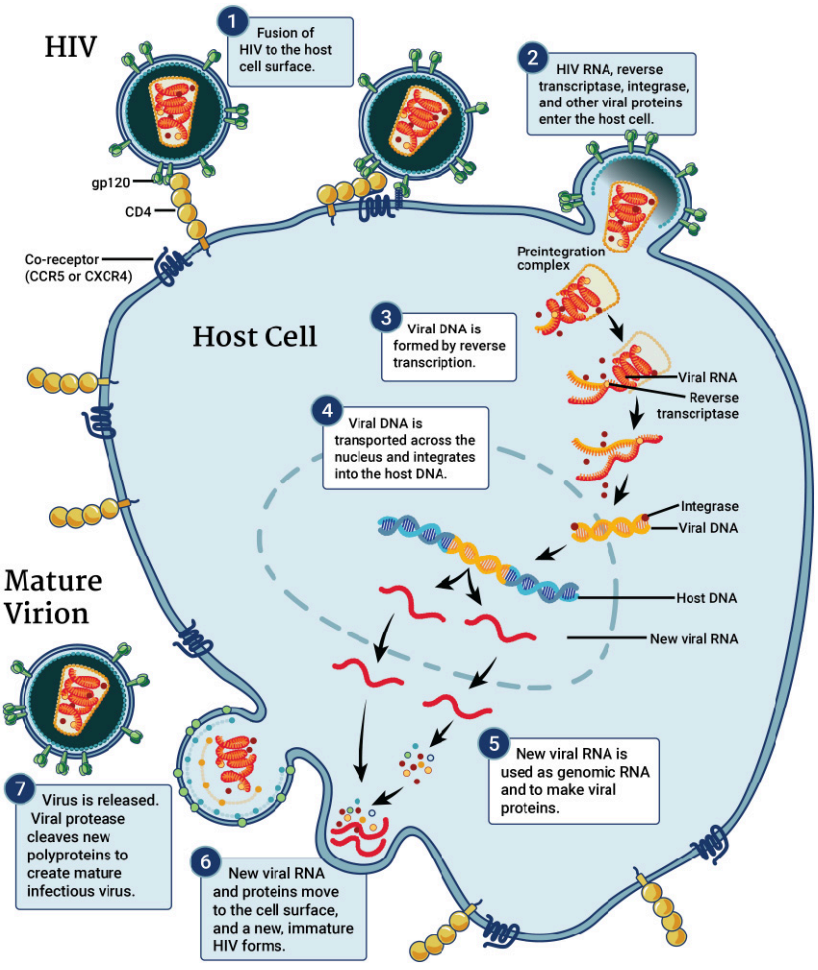


FIGURE 7.4 HIV attaches to the CD4 receptor of an immune cell and fuses with the cell membrane. Viral contents are released into the cell, where viral enzymes convert the single-stranded RNA genome into DNA and incorporate it into the host genome. (credit: "HIV Replication Cycle" by National Institute of Allergy and Infectious Diseases (NIAID)/Flickr, CC BY 2.0)

Clinical Manifestations

Upon initial infection, many individuals may have few to no symptoms. Early symptoms may mimic the symptoms of mononucleosis, including fever, enlarged lymph nodes, and fatigue. After several weeks, the virus enters a latent period, and the person becomes asymptomatic. This provides a false sense of security because the virus is continually replicating, and immune cell destruction is occurring steadily. Once the client's CD4 cell count falls to

less than 200 cells/mL of blood, the client may present with an opportunistic infection such as PJP, which may be the first time the client is evaluated for HIV infection. Without HIV treatment, people with AIDS typically survive about 3 years due to complications caused by opportunistic infections and malignancies. People who are treated for HIV in stage one or two may never move into stage three. Without HIV treatment, stage two may last a decade or longer. At the end of this stage, the viral load of HIV in the blood increases and the person may move into stage three (AIDS).

HIV Transmission

HIV transmission can occur in different ways. Many bodily fluids from an infected individual, including blood, breast milk, semen, and vaginal fluids, contain the virus. These fluids can then be transmitted to an uninfected person via unprotected sexual intercourse, sharing of contaminated needles during injection drug use, or perinatal transmission from a pregnant client to their fetus. The type of sexual exposure can also affect the possibility of transmission of the virus to uninfected individuals. The risk of transmission is low during oral intercourse. Transmission rates are higher for penile–vaginal intercourse, and anal intercourse, especially receptive anal intercourse, carries the highest risk for transmission.

One factor that may influence the risk for viral transmission is the infected individual's **viral load**, or the number of copies of the viral RNA that are measured in the blood. The higher the viral load in the blood, the more likely the infected individual's fluids will contain copies of the virus capable of infecting another individual. This is why viral suppression with ART can help prevent the spread of HIV, along with other techniques such as using condoms and clean needles.

Laboratory Testing

Testing for and diagnosing HIV infection can be done with several types of tests, including antibody tests, antigen/antibody tests, and nucleic acid tests. The first two tests look for the presence of antibodies against the virus that the body has produced; therefore, the test may be negative if the client was recently infected and has not had time to develop antibodies. The nucleic acid test looks for copies of the viral RNA and can detect the presence of HIV sooner than antibody-based tests can. It is important for high-risk individuals (e.g., those who share needles, those who have unprotected sex with multiple partners) to be screened more often for HIV to ensure early diagnosis because treatment with ART can preserve immune function for as long as possible.

Two primary laboratory tests are used to track the efficacy of ART in HIV-infected individuals. The first is the viral load, which is a measure of how actively the virus is reproducing itself. The second is the CD4 cell count, which shows the degree of immune system degradation that has occurred and the degree of risk for developing opportunistic infections. Ideally, under ART treatment, the HIV viral load will be undetectable, and the CD4 cell count will be 500–1600 cells/mm^3. The CD4 cell is a type of white blood cell that plays a key role in the immune system by alerting other immune cells to the presence of infections in the body.

Testing can also be performed to determine the sensitivity or resistance to a variety of ART drugs. This is helpful to make sure that any treatment the client is receiving will be able to sufficiently suppress viral replication. HIV is prone to making mistakes when it copies itself, which leads to frequent mutations that induce resistance to various ART drugs, so sensitivity testing is critical to choosing an effective regimen.

Antiretroviral Drugs

Treatment of HIV is an ever-evolving subject, with guidelines frequently recommending different preferred ART regimens based on up-to-date research. The best place to get accurate, timely recommendations for ART is through the National Institutes of Health's HIV information website (https://openstax.org/r/hivinfo). For effective ART, multiple drugs utilizing different mechanisms of action are used together to synergize and suppress viral replication. The client's adherence is critical to achieve viral suppression and preserve their immune function. Nonadherence will often lead to viral resistance against ART drugs. Choosing combination products that reduce the number of pills a client takes in a day can help decrease regimen complexity and increase adherence.

Integrase Strand Transfer Inhibitors

Integrase strand transfer inhibitors (integrase inhibitors) include the drugs raltegravir, dolutegravir, and elvitegravir. They work by inhibiting the HIV enzyme integrase to prevent HIV DNA from being incorporated into the individual's

DNA. This then prevents the production of new copies of the virus. Integrase inhibitors are a relatively new class of drugs used in the treatment of HIV; given their efficacy and favorable tolerability, they have become components of many first-line regimens recommended for clients newly diagnosed with HIV.

Fusion Pump Inhibitors

The fusion pump inhibitor enfuvirtide works by preventing the fusion of the HIV virus with a CD4 cell. This prevents the cell from being infected and suppresses viral replication. Enfuvirtide is usually reserved for clients with treatment-resistant HIV because the drug must be injected subcutaneously twice daily and is quite costly.

Protease Inhibitors

Once HIV has integrated itself into the host cell's DNA, it begins to produce copies of viral proteins. These are produced in one long chain and must be cleaved via the enzyme protease to form functional, mature proteins. The use of protease inhibitors, such as atazanavir, darunavir, fosamprenavir, and ritonavir, keeps those proteins from maturing, and viral replication is suppressed.

Chemokine Coreceptor (CCR5) Antagonists

During the fusion process, some variants of HIV will look for the C-C chemokine receptor type 5 (CCR5) that lies on the cell surface to help the virus enter the cell. This protein plays a major role in inflammation by recruiting and activating leukocytes. CCR5 is also the principal HIV coreceptor and is involved in the pathology of both cancer and neuroinflammation. In addition, it has been implicated in the inflammatory complications of coronavirus disease 2019 (COVID-19). Maraviroc is a CCR5 antagonist that blocks this receptor to discourage fusion and entry of HIV into the cell. If the HIV that the client is infected with does not express the protein looking for the CCR5 receptor, then this drug will be ineffective.

Cytochrome P-450 Inhibitors

One way to increase blood levels of certain ART medications and reduce the number of pills a client takes in a day is by inhibiting CYP3A4. The two drugs used for this purpose are cobicistat and the protease inhibitor ritonavir. Inhibiting CYP3A4 reduces drug metabolism and boosts the blood levels of several antiretrovirals.

CLINICAL TIP

Double-Check for Drug Interactions, Including CYP Interactions

CYP3A4 inhibitors are useful to help reduce the number of pills a client needs to take and thus simplify their medication regimens. These inhibitors can also be the source of many drug interactions, including medications used for tuberculosis, high cholesterol, and bacterial infections. Nurses should always inspect a client's medication history to determine whether any changes to their current medications are necessary to avoid drug toxicity.

Non-nucleoside Reverse Transcriptase Inhibitors

Reverse transcriptase takes the viral RNA and makes a complementary copy of DNA that can then be integrated into the host cell DNA. By inhibiting reverse transcriptase, viral replication can be suppressed. One way to inhibit reverse transcriptase is by directly binding to it to affect its conformational shape and reduce its ability to produce DNA. This class of drugs is known as the non-nucleoside reverse transcriptase inhibitors (NNRTIs) and includes the drugs delavirdine, efavirenz, etravirine, and rilpivirine.

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors

An alternative way to inhibit reverse transcriptase is by using drugs that look like the nucleosides/nucleotides that are normally incorporated into viral DNA but that are modified to function as chain terminators to prevent DNA chain elongation. These drugs are called the nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and include the drugs abacavir, didanosine, tenofovir, and zidovudine. These agents serve as the backbone to many ART regimens. The NRTIs are ineffective as a monotherapy due to rapid resistance. First-line antiretroviral regimens include two NRTIs and one other drug from a different class, such as NNRTIs or protease inhibitors. Today, treatment has become simplified due to the availability of combination agents. This simplified regimen enhances adherence.

Table 7.9 lists antiretroviral drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Atazanavir (Reyataz)	300 mg orally once daily with or without boosting with ritonavir.
Cobicistat (Tybost)	150 mg orally once daily.
Dolutegravir/rilpivirine (JULUCA)	50 mg of dolutegravir and 25 mg of rilpivirine once daily.
Enfuvirtide (Fuzeon)	2 mg/kg/dose subcutaneously twice daily; maximum dose: 90 mg/dose.
Etravirine (Intelence)	200 mg orally twice daily.
Raltegravir (Isentress)	400 mg orally twice daily.
Tenofovir (Viread)	300 mg orally once daily.

TABLE 7.9 **Drug Emphasis Table: Antiretroviral Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Antiretroviral agents are known to cause gastrointestinal discomfort, including nausea, vomiting, and diarrhea. A contraindication to any antiretroviral drug is known hypersensitivity.

The most common adverse effects associated with enfuvirtide include fatigue, diarrhea, and injection site reactions.

Common adverse effects among the protease inhibitors include liver injury and metabolic disorders such as dyslipidemia and glucose intolerance.

SAFETY ALERT

Protease Inhibitors

Effective ART therapy has allowed many clients with HIV to live decades longer than they might have if diagnosed in the 1980s. Protease inhibitor use, however, can increase the risk for metabolic complications in these clients, including raising serum glucose and lipid levels. This may predispose them to conditions such as diabetes and atherosclerotic cardiovascular disease (e.g., angina, myocardial infarction). As these clients age, health care professionals should screen for these metabolic conditions to be able to intervene before complications develop.

The main adverse effects seen with maraviroc are gastrointestinal upset and upper respiratory infection.

Common adverse reactions to the NNRTIs include rash, insomnia, and liver injury. Use of this class of drugs is on the decline due to poor tolerability and safety issues.

Older, first-generation NRTIs such as didanosine and zidovudine are more frequently associated with adverse effects such as peripheral neuropathies, pancreatitis, and lactic acidosis. Newer agents such as abacavir and tenofovir tend to be better tolerated and are included in many of the recommended regimens for HIV treatment.

Table 7.10 is a drug prototype table for antiretroviral drugs featuring dolutegravir/rilpivirine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Integrase strand transfer inhibitor **Mechanism of Action** Binds to the integrase active site and inhibits the strand transfer step of HIV DNA integration necessary for HIV replication	**Drug Dosage** 50 mg of dolutegravir and 25 mg of rilpivirine once daily.
Indications HIV infection **Therapeutic Effects** Suppresses HIV replication and preserves the immune system	**Drug Interactions** Aluminum hydroxide Carbamazepine Dofetilide Efavirenz Fosamprenavir **Food Interactions** Dairy products
Adverse Effects Increased serum lipase Pruritis Hyperglycemia Abdominal distress Hepatitis	**Contraindications** Hypersensitivity Caution: Hepatotoxicity Immune reconstitution syndrome

TABLE 7.10 **Drug Prototype Table: Dolutegravir/Rilpivirine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antiretroviral drugs:

- Monitor for signs and symptoms of anaphylaxis (e.g., shortness of breath, difficulty breathing, difficulty swallowing).
- Advise the client to take the entire prescribed course of the drug to ensure adequate treatment and to reduce the development of drug resistance.
- Teach the client to monitor for symptoms of lactic acidosis (e.g., abnormal heartbeat, muscle cramps, abdominal pain).
- Educate about sterile, proper injection technique if the client is using enfuvirtide.
- Monitor for potential CYP3A4 interactions with other medications the client is taking if they are using ritonavir or cobicistat.
- Monitor for liver dysfunction in clients receiving maraviroc.
- Evaluate for the presence of the HLA-B*5701 genetic mutation before beginning abacavir because its presence increases the risk for anaphylaxis.
- For clients receiving protease inhibitors, monitor for changes in serum lipids and glucose to reduce the risk for heart disease.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antiretroviral should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should *not* take double doses.

- Alert their health care provider about any adverse effects or barriers to taking the medication correctly to ensure adherence and appropriate drug selection.
- Understand proper sterile injection technique to reduce the risk for infection.
- Report any rash or yellowish skin discoloration if they are taking maraviroc.
- Make sure to take every dose in their regimen to decrease the development of viral resistance.
- Make sure to practice safer sex (e.g., condom use, fewer sexual partners) and avoid sharing needles to reduce the chances of transmitting HIV.

FDA BLACK BOX WARNING

HIV and AIDS Medications

Abacavir: Serious and sometimes fatal hypersensitivity reactions, with multiple organ involvement, have occurred with abacavir. Clients who carry the HLA-B*5701 allele are at a higher risk for a hypersensitivity reaction to abacavir, although hypersensitivity reactions have occurred in clients who do not carry the HLA-B*5701 allele.

Maraviroc: Hepatotoxicity has been reported with use of maraviroc. Severe rash or evidence of a systemic allergic reaction (e.g., eosinophilia, elevated immunoglobulin E [IgE], fever) prior to the development of hepatotoxicity may occur. Clients with signs or symptoms of hepatitis or allergic reaction following use of maraviroc should be immediately evaluated.

7.4 Introduction to Sexually Transmitted Infections and Drugs to Treat Them

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 7.4.1 Describe the pathophysiology of common sexually transmitted infections.
- 7.4.2 Identify clinical manifestations related to common sexually transmitted infections.
- 7.4.3 Identify the etiology and diagnostic studies related to common sexually transmitted infections.
- 7.4.4 Identify various methods to prevent the transmission of sexually transmitted infections.
- 7.4.5 Identify the characteristics of drugs used to treat common sexually transmitted infections.
- 7.4.6 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat common sexually transmitted infections.
- 7.4.7 Describe nursing implications of drugs used to treat common sexually transmitted infections.
- 7.4.8 Explain the client education related to drugs used to treat common sexually transmitted infections.

According to the World Health Organization, more than 1 million **sexually transmitted infections (STIs)** are acquired every day (2023b). Many of these are asymptomatic, which accounts for their rapid spread between sexual partners. The consequences of not appropriately preventing, screening for, and treating STIs are numerous and include complications such as infertility, cancer, pregnancy complications, and increased risk for HIV infection. Due to the societal stigma around STIs, many people may be hesitant to seek out care for STIs because of perceived judgement from friends, family, and health care professionals. Nurses should always adopt a curious, nonjudgmental approach with clients to encourage open and honest communication so that clients get the care they need and deserve.

Bacterial Infections

Bacteria are known to cause several STIs, and they respond well to antibiotics covered previously in this chapter. One ongoing concern with the treatment of bacterial STIs is the development of drug-resistant bacteria that do not respond to traditional therapies. Health care professionals should follow the latest clinical guidelines from the Centers for Disease Control and Prevention (https://openstax.org/r/cdcgovstd).

Bacterial Vaginosis

Bacterial vaginosis (BV) is a common cause of vaginal discharge and occurs when the normal bacterial flora of the vagina shift from the normally dominant lactobacilli to other pathogenic species. Disruption of the normal vaginal

flora can occur for a variety of reasons, but sex with multiple partners, douching, and not using condoms are cited as the most common risk factors. Individuals with BV may be asymptomatic or can have signs and symptoms such as vaginal discharge and fishy odor. Treatment is necessary to prevent outcomes such as acquisition of other STIs, pelvic inflammatory disease (PID), and preterm delivery if pregnant.

Chlamydia

Chlamydia is one of the most reported STIs in the United States, with more than 1.6 million cases being reported in 2021 (CDC, 2023a). The condition is caused by the organism *Chlamydia trachomatis*, which can spread during sexual intercourse. Clients with chlamydia may present with painful urination and urethral discharge in males or vaginal discharge in females. However, many affected individuals are asymptomatic and are diagnosed only if screened. Screening usually includes a nucleic acid amplification test (NAAT) to look for the presence of the organism. Untreated cases of chlamydia can progress to PID in female clients, which may result in chronic pain and infertility.

Gonorrhea

Gonorrhea is the second most reported STI in the United States, with over 700,000 cases being reported in 2021 (CDC, 2023a). The condition is caused by *Neisseria gonorrhoeae*, which is transmitted during sexual contact. As with chlamydia, some clients will remain asymptomatic, which aids in the spread to sexual partners. The most common presenting symptoms include mucopurulent penile discharge and painful urination. Diagnosis is made using a NAAT to look for presence of the organism. Complications from untreated cases of gonorrhea include PID, infertility, and increased risk for HIV infection.

Syphilis

Syphilis is a bacterial infection caused by the spirochete *Treponema pallidum*. It can be transmitted perinatally and through sexual contact. Syphilis can present in a variety of ways depending on the stage to which it has advanced. Primary syphilis is associated with a painless chancre on tissue that was exposed to the organism (usually the genital tissue). Secondary syphilis occurs as the organism spreads through the lymph system, producing skin lesions throughout the body. The third stage of syphilis is the latent phase, when the symptoms of the secondary stage disappear. In the most advanced stage, the organism can invade the body's organ systems, including the central nervous system (neurosyphilis) and the cardiovascular system (cardiovascular syphilis) and can result in stroke, seizures, vision problems, and death. Several tests can be performed to diagnose syphilis; the rapid plasma reagin (RPR) and venereal disease research laboratory (VDRL) tests are the most common.

TRENDING TODAY

Increasing Rates of STIs

The CDC tracks STI rates year to year and documented over 2.5 million cases in 2021, which is a marked increase from 2020 (CDC, 2023b). Although rates rose in all parts of the United States, certain populations were disproportionately affected, including gay and bisexual males; and females who belong to racial and ethnic minorities. The changes included more cases of gonorrhea and chlamydia and a 32.5% increase in congenital syphilis cases. Congenital syphilis occurs when an infant acquires the infection in utero from the birthing parent, and it is a cause of stillbirths and infant deaths. The CDC has called for an increased commitment to educating, preventing, and treating these infections to help reverse this trend. All health care professionals should be able to discuss sexual health topics with clients to increase disease awareness and teach them about safe practices to help prevent future cases of STIs.

Viral Infections

Viruses cause some STIs and may exist alongside the various bacterial organisms discussed previously. Unlike bacterial STIs, most of the viral STIs do not have definitive curative therapy, meaning these infections may become lifelong conditions to manage.

Herpes Simplex

Herpes simplex virus (HSV), discussed earlier in the chapter, is a major cause of genital ulcerations in the United States, with an estimated 572,000 cases reported each year (CDC, 2021). Despite its prevalence, many individuals

are asymptomatic, leading to transmission of the condition without the person's knowledge. Ulcerations are often painful and can occur in multiple episodes per year in susceptible individuals. Individuals with HSV infection are also more susceptible to HIV infection.

Human Papillomavirus

Human papillomavirus (HPV) is a DNA virus that spreads through skin-to-skin contact. HPV infection is also prevalent; an estimated 42.5 million people contracted the virus in 2018 (CDC, 2021). Most individuals who contract HPV remain asymptomatic; however, the signs and symptoms include genital warts, which can produce varying levels of discomfort. Many subtypes of HPV exist and are linked to different types of cancer, including cervical, anal, vaginal, and oropharyngeal cancers. This association prompted development of an HPV vaccine that protects against nine strains of the virus. The vaccine protects against cervical, vulvar, and vaginal cancer in females along with anal cancer and genital warts in both females and males.

Other Pathogenic Infections

A variety of other microorganisms are responsible for STIs, including trichomoniasis, a genitourinary infection that is caused by the protozoan parasite *Trichomonas vaginalis.* It is the most common nonviral STI; the CDC estimated that 6.9 million cases occurred in 2018 (CDC, 2021). Trichomoniasis infections are spread through sexual contact and typically present with purulent vaginal discharge and painful urination. As with many other conditions discussed, untreated trichomoniasis can lead to PID, infertility, and increased risk for HIV infection. A NAAT is available for screening clients for trichomoniasis to aid in diagnosis.

Preventing Transmission of STIs

Preventing STI transmission is the single best step individuals can take to protect their sexual health. Several strategies are available and should be discussed with clients to help prevent future infections from occurring. The most important way to prevent the spread of STIs is through education. Nurses should teach clients how STIs are transmitted and how they prevent infections.

STIs can be transmitted to anyone who has sexual contact (oral, vaginal, anal) with an infected individual, so one way to prevent transmission is to reduce unprotected contact. Correct and consistent use of barrier methods of protection, such as condoms, can reduce the risk for STI transmission. Clients should be instructed to use either latex or polyisoprene condoms because lambskin condoms are too porous to prevent the transmission of many organisms that cause STIs. Routine screening for individuals who do not use barrier methods of protection or who have multiple sexual partners can also detect STIs earlier, allowing earlier treatment and prevention of asymptomatic transmission to other individuals. Reducing the number of sexual partners can also decrease the risk for transmission. Finally, vaccination can help prevent several STIs, including HPV and HBV infections. Vaccines should be given before the onset of sexual activity because they will have little efficacy if the client has already been infected.

When diagnosed with an STI, the client should be encouraged to have their sexual partners tested as well because many infections may be asymptomatic. In addition, an asymptomatic infection may serve as a reservoir for transmission back to the client or to other sexual partners. Clients should also be educated to refrain from sexual activity while being treated for an STI to prevent transmission.

Communicating with Partners

Communication between sexual partners plays a crucial role in preventing the spread of STIs and promoting sexual health. Open and honest discussions about sexual history, testing, and protection methods are essential to maintaining a safe and responsible sexual relationship. By communicating openly, partners can share information about their STI status, discuss previous experiences, and make informed decisions together about contraception and safer sex practices. It is important for nurses to help create a nonjudgmental and supportive environment in which individuals feel comfortable discussing their sexual health concerns and seeking appropriate medical care when needed.

SPECIAL CONSIDERATIONS

Sexually Transmitted Infections

Health equity refers to the equal chance of every person to be healthy regardless of race, ethnicity, income, gender, religion, sexual identity, or disability. Unfortunately, data have shown that certain groups are more prone to STIs and encounter various structural and cultural barriers that prevent them from accessing the care they deserve (Norris et al., 2019). Notable groups disproportionately affected by STIs include females and some members of ethnic and racial minority groups. The reasons for this disparity are complex and multifactorial but include having insufficient financial support to access health care, being generally distrustful of the health care system, and being sexually active in communities in which sexual partners are more likely to have an STI. No single health care professional will be able to fix these problems, but they can educate and foster open and honest communication with their clients. This includes teaching them strategies to reduce the risk for acquiring an STI, directing the client to resources for preventive devices such as condoms, and fostering a nonjudgmental environment to encourage client honesty about their sexual health.

(Source: CDC, 2023c)

Drugs to Treat STIs

A variety of drugs are used to treat STIs in clinical practice; many were discussed in the previous sections. This section presents the agents that are appropriate for specific STIs and the concerns regarding resistance issues that have developed over time.

Antimicrobials

The ideal antimicrobial to treat an STI is one that is effective, has few adverse effects, is inexpensive, and can be given as a single dose or short course to ensure adherence. However, drug resistance continues to be problematic for drugs used to treat STIs. Therefore, nurses should make sure to regularly review current guidelines for the treatment of STIs. The following are common antimicrobials used to treat STIs:

- *Metronidazole:* Metronidazole has good activity against anaerobic bacteria and protozoa. For this reason, metronidazole is recommended for treatment of BV and trichomoniasis. The client's sexual partners should also be treated with metronidazole to prevent reinfection. Metronidazole may be given either orally or as a vaginal gel.
- *Clindamycin:* Clindamycin is an alternative treatment for BV if metronidazole cannot be used. It can be given orally or as a vaginal cream. Oral options are less preferred due to the risk for *C. difficile* infection and severe diarrhea.
- *Penicillin:* Penicillin is considered the treatment of choice for syphilis. It can be given as a single-dose, long-acting intramuscular injection to assist with client adherence. Continuous intravenous infusion may be necessary to treat neurosyphilis.
- *Ciprofloxacin:* Ciprofloxacin is a fluoroquinolone antibiotic that has some activity against *N. gonorrhea* and *C. trachomatis*. Due to fluoroquinolone overuse, antimicrobial resistance is a major issue with continued use of this drug, and guidelines list ciprofloxacin only as an alternative agent if clients cannot receive other first-line therapies such as ceftriaxone or doxycycline. Clients should be educated to avoid taking ciprofloxacin with any multivitamins or dairy products because iron and calcium can bind to the drug and render it ineffective.
- *Ceftriaxone:* Ceftriaxone is the treatment of choice for gonorrhea. It can be given as a single intramuscular injection for most cases of uncomplicated gonorrhea. The main adverse effect expected with this treatment is pain at the injection site, which can be offset by mixing ceftriaxone with a local anesthetic such as lidocaine.
- *Doxycycline:* Doxycycline is a tetracycline antibiotic that is the treatment of choice for chlamydia. Single doses of the macrolide azithromycin used to be the preferred therapy, but due to rising chlamydial resistance, doxycycline is now considered first-line therapy. The downside of doxycycline is that it must be given twice daily over 7 days, so nurses should impress upon the client the need to take all doses to prevent treatment failure and to control resistance.

SAFETY ALERT

Doxycycline

It is important to educate clients using doxycycline to avoid taking the medication with calcium- or iron-containing products to ensure absorption. Clients should also be instructed to avoid prolonged sun exposure and to use appropriate sun protection (e.g., physical coverings, sunscreen) to prevent sunburn.

- *Erythromycin:* Erythromycin is a macrolide antibiotic that can be used for treating neonatal gonococcal and chlamydial infections acquired perinatally from the birthing parent. Known or suspected infections can be treated with systemically administered erythromycin, and ophthalmic ointment administered to newborns as prophylaxis is standard of care in many U.S. hospitals. Approximately 1 cm in length of ointment should be administered into each lower conjunctival sac. The ointment should not be flushed from the eye following instillation. A new tube should be used for each infant.

Antivirals

Although not curative for any viral STIs, the antivirals acyclovir, valacyclovir, and famciclovir are used to help manage the symptoms of HSV and prevent spread to sexual partners. Nurses should inform clients taking antivirals for STIs that even if they do not have active lesions, viral shedding can still occur and thereby spread the infection to partners. If clients are taking antivirals for episodic management of HSV-related lesions, they should begin therapy within 24 hours of symptom onset to ensure drug efficacy. Chronic suppressive therapy, in which clients take the medication every day regardless of symptom status, can help prevent spread to sexual partners, but nurses should instruct clients to use additional protective measures such as condoms if the partner does not have HSV.

Table 7.11 lists commonly used medications to treat STIs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Acyclovir (Zovirax)	*Herpes simplex virus, mucocutaneous infection:* 400 mg orally 3 times daily for 7–10 days.
Ceftriaxone (Rocephin)	*Gonococcal infection:* 500 mg intramuscularly once.
Clindamycin (Cleocin)	*Bacterial vaginosis:* 300 mg orally twice daily for 7 days.
Doxycycline (Vibramycin)	*Chlamydia:* 100 mg orally twice daily for 7 days.
Metronidazole (Flagyl)	*Trichomoniasis:* 500 mg orally twice daily for 7 days.
Penicillin G benzathine (Bicillin L-A)	*Syphilis:* 2.4 million units intramuscularly once.

TABLE 7.11 **Drug Emphasis Table: Medications Used to Treat STIs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking medications for STIs:

- Monitor for signs and symptoms of anaphylaxis (e.g., shortness of breath, difficulty breathing, difficulty swallowing).
- Advise the client to take the entire prescribed course of the drug to ensure adequate treatment and to reduce the development of drug resistance.
- Instruct the client to maintain adequate hydration; monitor kidney function for renally eliminated medications such as penicillin and ciprofloxacin.
- Educate about safer sex practices and ways to avoid STIs in the future.
- Mix ceftriaxone with lidocaine, as ordered, to reduce the pain of intramuscular injections for treatment of gonorrhea.

- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a medication for an STI should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should *not* take double doses.
- Avoid consuming alcohol when receiving metronidazole/tinidazole treatment.
- Avoid taking ciprofloxacin or doxycycline with iron- or calcium-containing products because they will prevent the drug from being absorbed.
- Use sunscreen or protective coverings while out in the sun to prevent rash or sunburn when taking doxycycline.
- Refrain from sexual activity while taking medications for an STI.
- Use barrier methods such as condoms to help prevent transmission of HSV because transmission can occur even when no active lesions are present.
- Encourage all sexual partners to be tested as well to determine whether they also require treatment.

7.5 Introduction to Tuberculosis and Antitubercular Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 7.5.1 Describe the pathophysiology of tuberculosis.
- 7.5.2 Identify clinical manifestations related to tuberculosis.
- 7.5.3 Identify the etiology and diagnostic studies related to tuberculosis.
- 7.5.4 Identify the characteristics of drugs used to treat tuberculosis.
- 7.5.5 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat tuberculosis.
- 7.5.6 Describe nursing implications of drugs used to treat tuberculosis.
- 7.5.7 Explain the client education related to drugs used to treat tuberculosis.

Tubercular Infections

Tuberculosis (TB) is a deadly respiratory infection primarily caused by the organism *Mycobacterium tuberculosis*. Worldwide, TB is the second leading cause of infectious deaths after COVID-19 (World Health Organization, 2023a). Although TB is less of a concern in high-income nations, it is still a major cause for concern in lower-income nations and in clients at greater risk, including those who are immunocompromised and those living in close contact with other people (e.g., prisons, shelters, nursing homes). TB has been found to disproportionately affect marginalized racial and ethnic groups who already have limited access to health care and are most susceptible to the devastating effects of TB (CDC, 2018).

M. tuberculosis is a slow-growing mycobacterium that possesses a cellular envelope made up of mycolic acid, which makes it difficult for conventional antibiotics to penetrate and inhibit cellular growth. After an individual inhales aerosol droplets containing *M. tuberculosis*, they may either clear the organism immediately, develop an active TB infection, or develop latent TB, in which the organism goes into a dormant state. Latent TB can reside in the person's lungs for years, waiting to activate either spontaneously or through an episode of immunosuppression that can be brought on by conditions such as HIV, diabetes, end-stage kidney disease, or the use of corticosteroids (e.g., dexamethasone, prednisone).

Individuals with TB typically present with common signs and symptoms, including weight loss, fatigue, productive cough, fever, and night sweats. Other signs and symptoms may include chest pain and hemoptysis (coughing up of blood). The health care provider should order a chest x-ray and then sputum samples if the x-ray shows infiltrates

suggestive of TB. Common findings on chest x-ray in clients with TB include mediastinal lymphadenopathy, pleural effusion, and pulmonary consolidation. Cases of latent TB are often screened for using tuberculin skin tests or interferon gamma release assay. Skin testing introduces tuberculin protein under the skin; redness and swelling (induration) at the injection site due to the presence of TB antibodies indicates latent TB infection. If clients show positive results from these tests, they will be referred for more diagnostic testing, including a chest x-ray to determine whether a latent infection is present.

First-Line Drug Therapy

Once a definitive diagnosis of TB has been made, treatment specific for TB should begin immediately. Due to the difficulty of drug penetration and the slow-growing nature of the organism, TB treatment requires at least 6 months of therapy. Failure to adhere to TB therapy can lead to clinical worsening in the client and more resistant strains of *M. tuberculosis.* Traditionally, clients with an active TB infection begin therapy with a four-drug regimen consisting of isoniazid, rifampin, pyrazinamide, and ethambutol for 2 months followed by 4 additional months of isoniazid and rifampin. The specific drugs used and their durations may be altered depending on client comorbidities and TB resistance.

CLINICAL TIP

Antitubercular Drug Compliance

Adherence to antitubercular drug regimens is critical to ensure eradication of the infection and prevention of drug-resistant strains of TB. One way to help ensure adherence is by using directly observed therapy, in which a trained observer watches the client take every dose of their TB medication. This can take place in the clinic, home care agency, correctional facility, or treatment center. Directly observed therapy helps provide stability and accountability and has been shown to increase antitubercular drug therapy completion. Directly observed therapy can even be completed electronically if that is more convenient for the client (Burzynski et al., 2022).

Drugs used to treat TB include:

- *Ethambutol hydrochloride:* Ethambutol inhibits RNA synthesis in susceptible mycobacteria to suppress cellular replication.
- *Isoniazid:* Isoniazid is an important component of the antitubercular regimen and works by inhibiting the production of mycolic acid. This inhibition disrupts the integrity of the mycobacterial cell wall, causing cell death.
- *Pyrazinamide:* Pyrazinamide is used during the first 2 months of therapy. Its mechanism for inhibiting *M. tuberculosis* is not fully known, but it is thought to reduce the pH of the local environment and discourage mycobacterial growth.
- *Rifamycins:* Rifampin, rifabutin, and rifapentine belong to the rifamycin class. These medications work to inhibit mycobacterial growth by binding to the enzyme RNA polymerase to reduce the cell's ability to produce new proteins, thereby stifling growth.

Drug Therapy for Multidrug-Resistant Tubercular Infections

Growing resistance to standard therapy is an ongoing concern for health care professionals managing TB. Health care providers should take care to select agents that the mycobacterium is susceptible to and weigh that efficacy against the adverse effect profiles of these agents. Selection should be based on sensitivity testing performed on samples collected from the client at the time of diagnosis and is made based on the discretion of an expert in infectious disease. Alternative agents include aminosalicylate sodium, capreomycin, ethionamide, and streptomycin. Resistant cases of TB should be referred to infectious disease specialists to ensure appropriate management of these complex cases.

Table 7.12 lists antitubercular drugs and typical routes and dosing for adult clients, along with the typical treatment times for standard TB regimens.

Drug	Routes and Dosage Ranges
Ethambutol (Myambutol)	800–1600 mg orally once daily for 26 weeks.
Isoniazid (Isovit)	300 mg orally once daily for 26 weeks.
Pyrazinamide (Rifater)	1–2 g orally once daily for 8 weeks.
Rifampin (Rifadin)	10 mg/kg (maximum dose: 600 mg) orally once daily for 8 weeks.

TABLE 7.12 **Drug Emphasis Table: Antitubercular Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Table 7.13 is a drug prototype table for antitubercular drugs featuring isoniazid. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antitubercular agent **Mechanism of Action** Inhibits synthesis of mycolic acids to disrupt the cell wall in *Mycobacterium tuberculosis*	**Drug Dosage** 300 mg orally once daily for 26 weeks.
Indications Active tuberculosis infection **Therapeutic Effects** Kills *M. tuberculosis* to eliminate infection	**Drug Interactions** Acetaminophen Alprazolam Dofetilide Dolutegravir Ketoconazole Nimodipine **Food Interactions** Ethanol Tyramine-containing foods
Adverse Effects Elevated serum transaminases Vasculitis Maculopapular rash Toxic epidermal necrolysis Nausea Agranulocytosis Bilirubinuria	**Contraindications** Hypersensitivity Acute liver disease Caution: Hepatic impairment Renal impairment

TABLE 7.13 **Drug Prototype Table: Isoniazid** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Antituberculosis medications are known to cause gastrointestinal discomfort, including nausea, vomiting, and diarrhea. A contraindication to any antituberculosis drug is known hypersensitivity.

Ethambutol is partially renally eliminated, so the dose should be adjusted in clients with renal dysfunction. The major adverse effects seen with ethambutol are optic nerve inflammation, changes in visual acuity, and loss of ability to distinguish between the colors red and green.

Isoniazid is a known hepatotoxin; serial liver function tests should be performed to determine whether therapy should be altered. Isoniazid also can cause neurotoxicity, including peripheral neuropathies at standard doses and seizures and coma in overdose. Clients particularly at risk for neurotoxicity include those who are pyridoxine deficient (e.g., pregnant clients, individuals with excessive alcohol intake).

SAFETY ALERT

Isoniazid

Nurses must inform clients that they should have their liver function assessed regularly while on isoniazid to monitor for liver toxicity. The client should also abstain from excessive alcohol use, which may increase the risk for hepatotoxicity. Excessive drinking includes binge drinking (4 or more drinks during a single occasion for females or 5 or more drinks during a single occasion for males) and heavy drinking (8 or more drinks per week for females or 15 or more drinks per week for males).

Pyrazinamide also is a known hepatotoxin, so serial liver function tests should be monitored for evidence of liver injury. In addition, pyrazinamide raises uric acid levels.

Rifampin and rifapentine are potent inducers of CYP3A4. These drugs can prove a challenging addition to a client's medication regimen because induction of CYP3A4 can speed the metabolism of affected drugs and lead to therapeutic failure. Medication profiles should be examined closely and adjustments made to account for the inclusion of rifampin and rifapentine. Rifabutin has much less CYP3A4 induction and causes fewer drug interactions, making it an alternative to rifampin. Rifampin can cause the client's secretions (e.g., urine, tears, sweat) to turn an orange to red color, which clients should be warned about before they start therapy. Rifampin is another TB drug that requires monitoring for elevations in liver function tests because it may worsen hepatic function.

Nursing Implications

The nurse should do the following for clients who are taking an antitubercular drug:

- Monitor for signs and symptoms of anaphylaxis (e.g., shortness of breath, difficulty swallowing, etc.).
- Advise the client to take the entire prescribed regimen to ensure adequate treatment and to reduce the development of drug resistance.
- Tell the client to report signs and symptoms of liver impairment (e.g., yellowish skin, vomiting, abdominal pain, dark urine) that may occur while clients are taking isoniazid, rifampin, or pyrazinamide.
- Screen clients using rifampin for any medication interactions and alert the health care provider as needed.
- Monitor uric acid levels as well as liver function tests for clients taking pyrazinamide.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antitubercular drug should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should *not* take double doses.
- Alert their health care provider about any visual changes, such as decreased ability to see certain colors, while on ethambutol.
- Alert their health care provider if they experience any signs of liver dysfunction, including yellowish skin, vomiting, abdominal pain, or dark urine.
- Be aware that their urine or sweat may appear red to orange while taking rifampin.
- Make sure to take every dose of their regimen to help ensure successful therapy, reduce drug resistance, and prevent the transmission of TB to others.
- Avoid excessive alcohol to avoid liver injury.
- Report to their health care provider any numbness or tingling in the extremities while taking isoniazid.

FDA BLACK BOX WARNING

Isoniazid

Severe and sometimes fatal hepatitis associated with isoniazid therapy has been reported and may occur or develop even after many months of treatment.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Mark Janson is a 36-year-old client who presents to the emergency department complaining of coughing up blood for the past 3 days. He reports intermittent fevers, chills, night sweats, and difficulty breathing that worsens on exertion. He notes that he has unintentionally lost 25 pounds over the last several weeks.

History
None

Current Medications
Acetaminophen 650 mg orally every 6 hours as needed for fever
Dextromethorphan 20 mg orally every 4 hours as needed for cough, which has not provided relief

Vital Signs		Physical Examination
Temperature:	98.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Within defined limits • *Cardiovascular:* No jugular vein distention; no peripheral edema noted bilaterally; S1, S2 noted, rhythm regular • *Respiratory:* Rhonchi and dullness to percussion in the right upper lobe, tachypneic, labored breathing • *GI:* Abdomen soft, nontender, nondistended • *GU:* Reports normal urine output • *Neurologic:* Within defined limits • *Integumentary:* No wounds noted; skin appropriate for age
Blood pressure:	135/73 mm Hg	
Heart rate:	100 beats/min	
Respiratory rate:	24 breaths/min	
Oxygen saturation:	93% on room air	
Height:	5'10"	
Weight:	154 lb	

TABLE 7.14

1. Based on the nurse's assessment, what is a priority question for the nurse to ask Mark?
   a. "Have you ever been tested for tuberculosis?"
   b. "Are you up to date on your tetanus shot?"
   c. "What is your sexual orientation?"
   d. "Are you employed?"

2. Which type of culture should the nurse anticipate if the client has tuberculosis?
   a. Bacterial
   b. Viral
   c. Mycobacterial
   d. Fungal

7.6 Antiparasitic and Anthelminthic Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 7.6.1 Describe the pathophysiology of common parasitic and helminthic infections.
- 7.6.2 Identify clinical manifestations related to common parasitic and helminthic infections.
- 7.6.3 Identify the etiology and diagnostic studies related to common parasitic and helminthic infections.
- 7.6.4 Identify the characteristics of drugs used to treat common parasitic and helminthic infections.
- 7.6.5 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat common parasitic and helminthic infections.
- 7.6.6 Describe nursing implications of drugs used to treat common parasitic and helminthic infections.
- 7.6.7 Explain the client education related to drugs used to treat common parasitic and helminthic infections.

Parasitic Infections

In the United States, **parasitic infections** can affect anyone, but they disproportionately affect immunocompromised individuals, members of racial and ethnic minority groups, and those with low income. Parasitic infections are defined by the relationship been the host (human) and the parasite. Common types of parasitic infections are caused by protozoa and helminths.

- **Protozoa**: Protozoa are unicellular organisms that replicate within a human host. Examples of protozoal infections include those caused by *Giardia, Plasmodium*, and *Babesia*. Many of these conditions affect clients living in areas with poor sanitation because the spread can be attributed to either fecal-contaminated water or fecal–oral transfer. Signs and symptoms of protozoal infections include diarrhea, low-grade fever, nausea, greasy stools, and depressed appetite. Intestinal protozoal infections are most often diagnosed from microscopic stool samples, although molecular tests have recently been developed that may allow faster detection of infections.
- **Helminths**: Helminths, or worms, are large complex organisms that can be consumed while they are in a larval stage and then mature into their adult stage in the host's gastrointestinal tract. Common signs and symptoms include abdominal pain and diarrhea; however, infections can also be asymptomatic. Similar to protozoal infections, microscopic examination of stool samples can reveal helminth eggs and aid in diagnosis.

Antiparasitic Drugs

This section covers the most frequently used antiparasitic drugs, including their mechanisms, adverse effects, indications, and contraindications. It is important to ensure that an accurate diagnosis has been made regarding the causative organism because this will dictate which medication is most appropriate for the client. Some of the most common antiparasitic drugs include:

- *Metronidazole:* For *Giardia lamblia, Trichomonas vaginalis, Cryptosporidium parvum*, and *Toxoplasmosis gondii*, metronidazole is the drug of choice. It provides good coverage against *Entamoeba, Giardia*, and *Trichomonas*, which are the species that cause infection.
- *Tinidazole:* Tinidazole is structurally related to metronidazole and has similar actions, adverse effects, and interactions. It also has a longer half-life than metronidazole, so dosing is more convenient. However, tinidazole is much more expensive than metronidazole. Tinidazole is contraindicated in clients consuming alcohol while using the drug due to risk for causing a severe flushing reaction.
- *Nitazoxanide:* Nitazoxanide is an alternative antiparasitic that can be used to treat giardiasis and cryptosporidiosis. Its full mechanism is unknown, but it is thought to disrupt the ability of these microorganisms to undergo anaerobic metabolism, leading to cell death. Nitazoxanide is well tolerated but can cause some gastrointestinal signs and symptoms.
- *Scabicides and pediculicides:* Scabicides and pediculicides are designed to treat infestations caused by lice and scabies. Lice, depending on the species, can cause symptoms on the head, body, or genitals. Collectively, this condition is known as pediculosis. Lice can be difficult to treat because if the eggs (nits) are not successfully removed from the hair after treatment, reinfestation can occur. Nit combs can be indispensable along with pediculicides. All agents in this category are applied topically to the affected area.

- *Permethrin:* Permethrin has a wide range of activity against a variety of arthropods, which makes it useful for lice infestations. Permethrin works by causing neuronal hyperpolarization and paralysis in the organism, leading to death.
- *Lindane:* Lindane has activity against lice and scabies and works by being absorbed into the parasite's exoskeleton, leading to seizures and death.
- *Malathion:* Malathion comes from a group of chemicals known as organophosphates, which have been used as agricultural insecticides for many years. It works by inhibiting the enzyme acetylcholinesterase, which is responsible for metabolizing acetylcholine. This causes a buildup of acetylcholine, leading to overstimulation, paralysis, and death of the parasite.
- *Spinosad:* Spinosad is another topical antiparasitic with activity against scabies and lice. It works by inducing neuronal excitation and eventual paralysis and death of the organism. The most common adverse effects seen with spinosad include redness and skin irritation at the application site.

CLINICAL TIP

Ensure Removal of Nits

Nits are the eggs of lice that attach to the hair, and they are unaffected by pediculicides. To ensure that nits do not go on to mature into adults requiring further pediculicide treatment, it is important to carefully comb through the hair with a fine-tooth nit comb after using a pediculicide. Shaving the head is a viable alternative, but this is not a desirable outcome for many clients.

Anthelminthic Drugs

The available anthelminthic agents are broad spectrum and can treat a variety of worms, including roundworms, pinworms, hookworms, and whipworms. Because worm infections occur in the gastrointestinal tract, these agents are taken orally.

- *Mebendazole:* Mebendazole works by inhibiting microtubule formation in susceptible helminths and blocking glucose uptake. This action leads to eventual death of the worm, after which it can be passed through the feces.
- *Ivermectin:* Ivermectin is an interesting antiparasitic agent because it has activity as both a pediculicide and an antihelminth. When used topically, it can treat lice and scabies infestations; when taken orally, it can treat a variety of helminth infections. Ivermectin works by inhibiting parasite nerve and muscle tissue, causing paralysis and death of the organism.

Table 7.15 lists antiparasitic and anthelminthic drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Lindane	*Head lice:* Apply 30–60 mL shampoo to dry hair and massage into hair for 4 min; add small quantities of water to hair until lather forms, then rinse hair and comb with fine-tooth comb to remove nits.
Mebendazole (Emverm)	*Ascariasis:* 100 mg orally twice daily for 3 days or 500 mg orally once daily.
Metronidazole (Flagyl)	*Giardiasis:* 250 mg orally 3 times daily for 5–7 days. *Trichomoniasis:* 500 mg orally twice daily for 7 days. *Amebiasis:* 500 mg orally every 8 hours for 7–10 days.
Nitazoxanide (Alinia)	*Giardiasis:* 500 mg orally every 12 hours for 3 days.
Permethrin (Elimite)	*Head lice:* Apply enough lotion or cream to saturate hair. Leave on for 10 min and then rinse with warm water.
Spinosad (Natroba)	*Head lice:* Apply sufficient amount to cover scalp.

TABLE 7.15 **Drug Emphasis Table: Antiparasitic and Anthelminthic Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Most oral antiprotozoal and anthelminthic drugs can cause gastrointestinal upset. Any topical scabicides and pediculicides may cause skin irritation to the area where they are applied. Excessive use of lindane is not recommended in high doses, especially in children, because it can cause central nervous system excitation and seizure. Malathion should be kept away from children because ingesting it could cause cholinergic poisoning.

Table 7.16 is a drug prototype table for antiparasitic and anthelminthic drugs featuring metronidazole. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nitroimidazole **Mechanism of Action** Causes loss of helical DNA structure and strand breakage to cause cell death	**Drug Dosage** *Giardiasis:* 250 mg orally 3 times daily for 5–7 days. *Trichomoniasis:* 500 mg orally twice daily for 7 days. *Amebiasis:* 500 mg orally every 8 hours for 7–10 days.
Indications Amebicide Antiprotozoal **Therapeutic Effects** Reduces symptoms of infection	**Drug Interactions** Disulfiram Fosphenytoin Haloperidol Mebendazole **Food Interactions** Ethanol
Adverse Effects Nausea Vaginitis Headache Abdominal pain Diarrhea Xerostomia Dizziness	**Contraindications** Hypersensitivity Caution: Superinfection Hepatic impairment Renal impairment Seizure disorder

TABLE 7.16 **Drug Prototype Table: Metronidazole** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antiparasitic or anthelminthic drugs:

- Monitor for signs and symptoms of anaphylaxis (e.g., shortness of breath, difficulty breathing, difficulty swallowing).
- Advise the client to take the entire prescribed course of the medication to ensure adequate treatment and to reduce the development of drug resistance.
- Instruct the client to maintain adequate hydration; monitor kidney function for renally eliminated medications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antiparasitic or anthelminthic drug should:

- Alert their health care provider about any signs of allergic reactions including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should *not* take double doses.

- Avoid taking tinidazole or metronidazole with alcohol because the interaction can cause a severe flushing reaction.

FDA BLACK BOX WARNING

Lindane Lotion

Seizures and deaths have been reported following repeated or prolonged use and in rare cases following a single application.

Chapter Summary

This chapter focused on a variety of infections caused by bacteria, viruses, fungi, and parasites. A brief review of the immune system was provided to explain the basic forms of defense the body uses to prevent infections as well as what happens when these defenses fail. Pharmacotherapy was reviewed, covering the most common antibiotics, antifungals, antivirals, and medications used to treat infections, including COVID-19, HIV, STIs, TB, and protozoal and helminthic infections. Mechanisms for the development of anti-infective resistance were discussed, including the fact that health care professionals must always be mindful of how they use anti-infectives to ensure their continued effectiveness in the future. The importance of client adherence was stressed, not only so the client can get the best treatment possible but also to help curb resistance. Given that some conditions are often associated with negative stigmas, nurses must strive to foster open and nonjudgmental environments in which clients from all backgrounds can feel comfortable getting the health care they deserve.

Key Terms

acquired immunodeficiency syndrome (AIDS) a group of conditions associated with immune system dysfunction caused by the human immunodeficiency virus

adaptive immunity the body's organism-specific defenses against infection

anti-infective stewardship the process of using anti-infectives judiciously to prevent drug resistance

antibiogram a document detailing local bacterial resistance patterns that is used to guide antibiotic choices

antiretroviral therapy (ART) medications designed to treat infections caused by the human immunodeficiency virus

apoptosis programmed cell death, usually due to cellular damage

bactericidal the ability to directly kill bacteria

bacteriostatic having the property of preventing bacteria from actively replicating, although not killing them directly

helminths worms capable of causing parasitic infections

human immunodeficiency virus (HIV) retrovirus that causes progressive immune system dysfunction

immunocompromised the state in which the immune system is unable to effectively prevent infection

innate immunity the body's nonspecific defenses against infection

parasitic infection infection caused by parasites—organisms that derive nutrition from their host while causing it harm

protozoa unicellular organisms capable of causing parasitic infections

sexually transmitted infection (STI) infections passed on via sexual forms of contact

superinfection infection caused by resistant bacteria after the use of broad-spectrum anti-infectives

tuberculosis (TB) a pulmonary infection caused by *Mycobacterium tuberculosis*

viral load the number of viral particles measured in a sample of body fluid or tissue (usually blood)

virologic cure sustained undetectable viral levels in the blood

Review Questions

1. A nurse is evaluating a client in the emergency department who presents with painful urination and urethral discharge. Laboratory tests indicate that the client is positive for gonorrhea. Which medication does the nurse anticipate the health care provider will most likely prescribe?

a. Ceftriaxone
b. Acyclovir
c. Metronidazole
d. Permethrin

2. A nurse is talking with a 17-year-old client who states they have heard about vaccines to prevent sexually transmitted infections. Which condition should the nurse tell the client is preventable with vaccination?

a. Hepatitis C
b. HIV
c. Human papillomavirus
d. Chlamydia

3. A nurse is counseling a client about their new tuberculosis diagnosis and the medications they will be taking. Which of the following educational points should the nurse make to the client?
   a. "Your urine may turn blue."
   b. "Follow up with the health care provider if you cannot tell the difference between green and red."
   c. "Missing doses every once in a while is not a problem."
   d. "There are no drug interactions to worry about with your tuberculosis medication."

4. A nurse is reviewing a client's medication profile and notices that they are taking isoniazid, rifampin, ethambutol, and pyrazinamide for tuberculosis. These drugs can affect the function of which of the following organ systems?
   a. Heart
   b. Lungs
   c. Muscle
   d. Liver

5. A nurse is examining a school-age child who is complaining of an itchy scalp. On physical examination, the nurse notices lice and nits in the child's hair. Which medication would the nurse anticipate being ordered to treat the child's lice infestation?
   a. Metronidazole
   b. Mebendazole
   c. Lindane
   d. Nitazoxanide

6. The nurse is caring for a client with HIV who is receiving antiretroviral therapy. Which laboratory value should the nurse assess to determine the competency of the client's immune system with this therapy?
   a. CD4 count
   b. HIV viral load
   c. Basophil count
   d. Neutrophil count

7. The nurse is teaching a client about their medications, which include elvitegravir, cobicistat, tenofovir, and lamivudine. Which medication would the nurse tell the client works by inhibiting integration of the HIV DNA into their own DNA?
   a. Cobicistat
   b. Elvitegravir
   c. Lamivudine
   d. Tenofovir

8. A client with a history of anaphylaxis to sulfonamides is being treated for a urinary tract infection. Which of the following medications is contraindicated in the care of this client?
   a. Metronidazole
   b. Ciprofloxacin
   c. Cephalexin
   d. Sulfamethoxazole

9. A client presents to the health care provider's office with a report of profuse watery diarrhea that started 10 days after they began taking clindamycin for a skin infection. Which organism does the nurse anticipate is responsible for the client's symptoms?
   a. *Staphylococcus aureus*
   b. *Pseudomonas aeruginosa*
   c. *Clostridioides difficile*
   d. *Streptococcus pneumoniae*

10. A client is being prescribed a tetracycline antibiotic for an upper respiratory tract infection. What would be an important educational point for the nurse to teach the client?

a. "Stop taking the medication when you begin to feel better."
b. "You can take the medication with milk, juice, or water."
c. "This medication is effective for bacterial and viral infections."
d. "Talk to your health care provider before becoming pregnant."

CHAPTER 8

Introduction to Cancer Therapy and Cancer Drugs

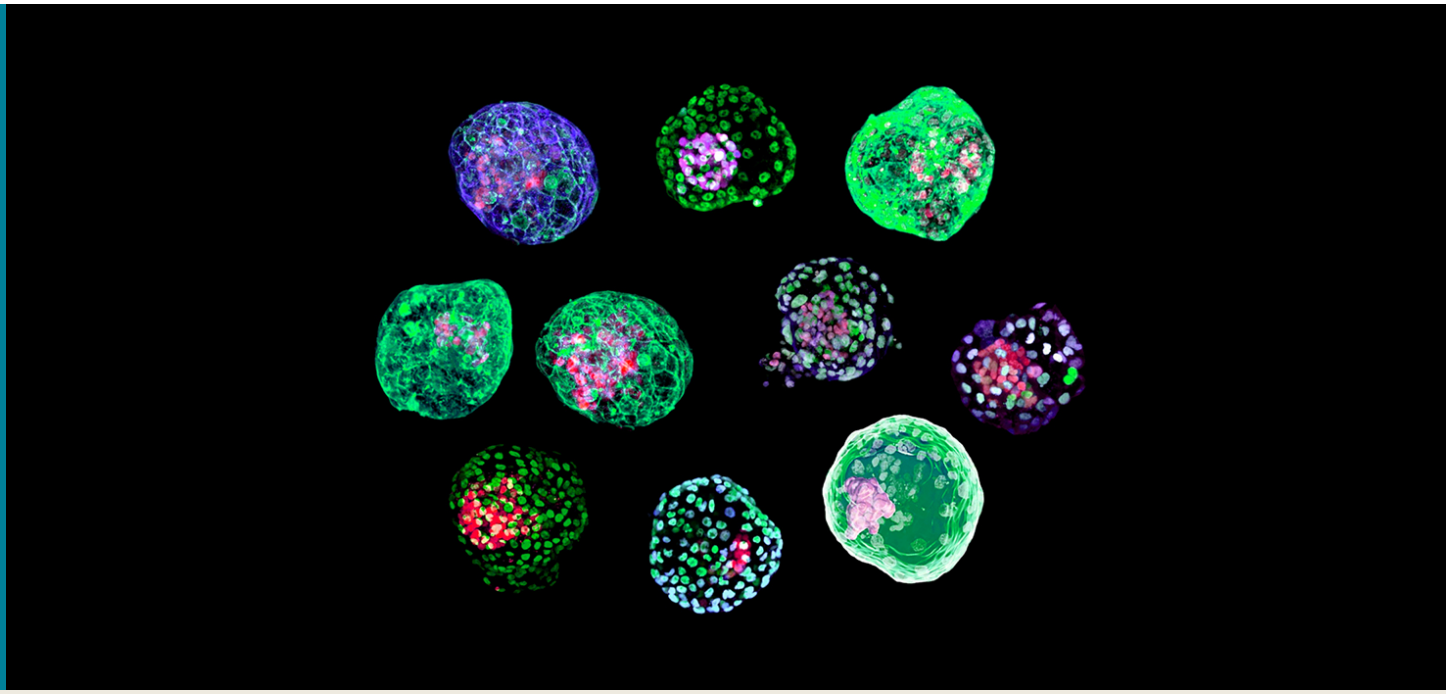


FIGURE 8.1 The immune system is a complex network of cells, tissues, and organs that work together to protect the body from harmful substances, such as pathogens. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license.)

CHAPTER OUTLINE

INTRODUCTION Cancer is a broad term used to describe the development of cell mutations that cause unrestricted cell growth, ultimately resulting in malignant neoplasms or tumors (**benign** overgrowths can also occur but will not be discussed in this chapter). These malignancies can occur in many areas of the body and can **metastasize**, or spread, to other sites from which the tumor originated.

Cancer care is a large part of the health care economy. However, when considering cancer care, nurses should be aware that there are many disparities in the provision of cancer care. Nurses should consider these disparities in order to understand the issues and challenges for clients and health care providers. Nurses must be client advocates to help negate those disparities in the care of clients with cancer. The National Cancer Institute provides substantial information about the disparities and effects on client care (https://openstax.org/r/cancergov).

8.1 Introduction to Cancer and Phases of Cancer Therapy

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 8.1.1 Describe cancer and cancer development.
- 8.1.2 Discuss contributing theories of environmental versus genetic etiologies of cancer development.
- 8.1.3 Identify the characteristics of cancer cells.
- 8.1.4 Describe different types of cancer.

Cancer Development

Each day, the human body experiences cell **mutations** that result in a change in cellular structure, which may lead to cancer development. When this happens, the intracellular machinery may be able to repair the mutation, or the body's immune system recognizes these cells as abnormal and attacks them. These are two innate defenses against cancer development. When either defense fails, cancer development can occur. There are multiple theories about the causes of cancer development. The most common theories are based on environmental exposures and genetic predispositions as causes of cancer development.

Environmental and Genetic Factors

Environmental exposures are outside factors that can cause cell mutations when the body is exposed to them. Most commonly, these factors include exposure to tobacco products, benzenes, petroleum-based products, asbestos, and certain drugs, including chemotherapies. There are many other substances that are classified as carcinogens, or cancer-causing agents. Somatic mutations occur from carcinogen exposures after birth. They do not develop from genetic mutations and do not affect germ cells that become ova and sperm.

LINK TO LEARNING

Environmental Exposure in a Community: Love Canal, New York

Access multimedia content (https://openstax.org/books/pharmacology/pages/8-1-introduction-to-cancer-and-phases-of-cancer-therapy)

One of the earliest findings of cancer and other diseases directly linked to environmental exposures occurred in the small community of Love Canal, Niagara Falls, in upstate New York. The story of Love Canal, while very unfortunate, brought about widespread change in environmental protection and regulation of toxic substances.

Genetic factors are those internal predispositions to cellular changes that result in cancer development. For example, clients who inherit the breast cancer **oncogenes** (BRCA1 and BRCA2) have a much higher chance of developing breast cancer than clients without these mutations (Centers for Disease Control and Prevention [CDC], 2020). These are considered to be germline mutations that develop in the eggs or sperm of a parent and are passed on to offspring.

LINK TO LEARNING

Oncogenes and Breast Cancer

Because genetic mutations that cause specific cancers to develop are present at birth, screening for the presence of some of these oncogenes (https://openstax.org/r/cdcgovgenomics) is now possible. When these oncogenes are identified before cancer has developed, clients now have options for improved surveillance and early detection and intervention. This promotes better outcomes for those clients who were born with hereditary gene mutations. The breast cancer antigen mutations 1 and 2 (BRCA1, BRCA2) are two of the most well-understood oncogenes.

Additional theories are based on immune system failure and the effects that physical and mental stress have on the body's ability to defend itself. Cell mutations occur frequently throughout the human body, but these cells are usually targeted and either repaired or destroyed by the immune system. When the immune system fails to

recognize mutated cells, these cells continue replication, forming a tumor. Other illnesses, physical stress, and mental distress are some factors that decrease the effectiveness of the immune-system functions. When considering theories of cancer development, most researchers agree that a combination of causative factors, rather than one single theory, contributes to cancer development (Mbemi et al., 2020).

Cellular Changes

Once a cancer-causing mutation occurs, if it is unable to be repaired, the mutated cells continue to divide, resulting in the development of a tumor or malignancy (see Figure 8.2). These cells lose many of the regulatory characteristics of normal cells, including contact inhibition and a regulated rate of mitosis. Tumors also have the property of **neoangiogenesis**, which is the ability to grow new blood vessels to support the metabolic needs associated with the abnormal growth. As these cells continue to grow, they can result in physical changes that greatly affect the function of the body.

Pain, compression, nutritional deficiencies, weight loss, and fluid and electrolyte imbalances are some of the effects that can occur with cancer development. However, tumors can also go unnoticed for many years. As growth continues, cancerous cells can metastasize to distant sites through direct extension into surrounding tissues, through seeding, and by **embolization** into the lymph and circulatory systems.

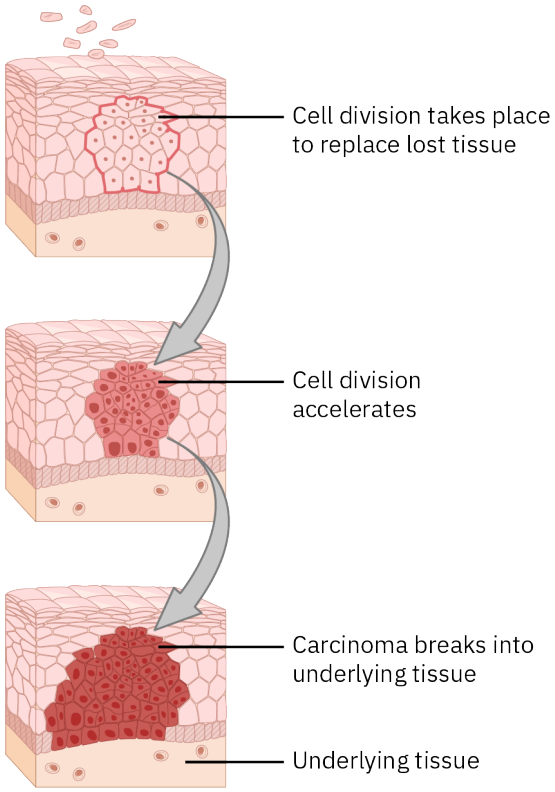


FIGURE 8.2 As cancer develops, there are changes in cell size, nucleus size, and organization of the tissue. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Cancer Types

Cancers are classified either by the type of tissue in which the cancer originates (histological type) or by the location in the body where the cancer originated (primary site) (National Cancer Institute, n.d.). Health care providers tend to refer to a cancer's histological type, while clients more frequently refer to the cancer's location. Many types of cancer will form tumors. Solid tumors are cancers that form in tissues of bones, skin, organs, and muscles. Liquid, or hematologic, tumors arise in the bone marrow and involve blood and lymphatic cells. Typically, regardless of tumor type, pharmacologic treatment will involve medications with systemic effects.

Solid Tumors

Solid tumors develop as a mass of cancer cells that originate in a specific area of the body. **Adenocarcinomas** and **squamous cell carcinomas** are two common pathological types of solid tumors. Adenocarcinomas develop in

glandular and epithelial tissues, while squamous cell carcinomas arise in the skin or in the lining of the respiratory and gastrointestinal system (National Cancer Institute, n.d.). Another type of solid tumor that is less common is a sarcoma. These tumors may form in soft tissues including fat, muscles, nerves, vessels, and skin. Sarcomas may also form in bones and most often affect young adults. In the United States, lung, prostate, and breast cancers are the leading causes of cancer-related mortality (National Cancer Institute, n.d.).

Hematologic (Liquid) Tumors

Hematologic cancers are cancers that arise in the bone marrow and involve blood cells, especially white blood cells and their precursors, and lymphocytes. These cancers are often called liquid tumors because they originate in the bone marrow and flow in the bloodstream. In the United States, **non-Hodgkin lymphoma**, **leukemia**, and **multiple myeloma** are the three most common hematologic cancers, respectively. These types of tumors present multiple issues because they exist in the vascular system, circulating through all parts of the body. When these cells are destroyed by chemotherapy, cellular debris and electrolytes are released into the blood. This may result in tumor lysis syndrome (TLS), a life-threatening condition that is characterized by acidosis, hyperkalemia, hyperphosphatemia, and hypocalcemia. When chemotherapy is given for a blood tumor in which high numbers of cancer cells are in the blood, clients must be pretreated with hydration therapy, allopurinol or rasburicase, and management of electrolytes. While tumor lysis occurs most commonly in hematologic cancers, it may occasionally occur with solid tumors that are very large and bulky.

LINK TO LEARNING

Tumor Lysis Syndrome

Tumor lysis syndrome is considered an oncologic or medical emergency, which without immediate recognition and treatment can result in fatal outcomes. The Cleveland Clinic has provided important updates about this syndrome (https://openstax.org/r/clevelandclinicorg) that can occur within hours of cancer treatment.

8.2 Chemotherapeutic Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 8.2.1 Identify principles of proper handling of chemotherapeutic agents.
- 8.2.2 Discuss different administration methods, phases, routes of administration, and types of chemotherapy.
- 8.2.3 Describe major side effects of chemotherapeutic agents.
- 8.2.4 Identify characteristics of different classes of chemotherapeutic agents used in cancer treatment.
- 8.2.5 Explain the indications, actions, adverse reactions, and interactions of chemotherapeutic agents used in cancer treatment.
- 8.2.6 Describe the nursing implications of chemotherapeutic agents.
- 8.2.7 Explain the client education related to chemotherapeutic agents.

Handling of Chemotherapeutic Agents

The complexity of administering **chemotherapy** and caring for clients that have been treated with cancer therapies requires advanced knowledge. Special training and certifications to administer chemotherapy are required. Chemotherapy agents may cause cytotoxic exposure to those who compound and administer these drugs as well as to clients, families, and other caretakers who might be exposed through spills, improper handling and disposal, and other means. Proper training in compounding, administering, and managing exposure emergencies is a requirement of all personnel who work with chemotherapy. Principles of appropriate handling include, but are not limited to, storage of cytotoxic substances in impervious containers, double gloving (chemotherapy-rated gloves), compounding in a negative-pressure hood, and disposing of cytotoxic substances based on national standards and institutional policies.

TRENDING TODAY

Chemotherapy Administration Safety Standards

The Oncology Nursing Society, a leader in developing oncology standards, developed chemotherapy administration guidelines and safety standards (https://openstax.org/r/onsorgonf) to assist nurses in safely administering chemotherapy and other cancer treatments. Advances in technology, cancer treatment, and nursing training prompted the need for a periodic review and revision of the standards for general oncology practices. The latest standards include pediatric oncology practices and new standards affecting chemotherapy prescription, preparation, and administration (Oncology Nursing Society, 2023).

Cancer Treatments

Chemotherapy may be given for many different reasons. Often, it is given as a curative measure to eradicate all malignant cells. However, cure is not always realistic. When cure is not attainable, chemotherapy can be used to decrease tumor size and prevent metastasis, and sometimes it may be used for palliation and symptom control. Differing regimens of chemotherapy are used for varying client needs (see Table 8.1).

Type of Therapy	Description
Adjuvant therapy	Given after initial treatment with surgery to destroy leftover cells
Neoadjuvant therapy	Initial treatment given to shrink the cancer before surgery
Salvage therapy	Second-line therapy given when first-line therapy is unsuccessful
Targeted therapy	Given to selectively kill cancer cells without harming normal cells
Biologic therapy	Used to enable the immune system to better kill cancer cells

TABLE 8.1 Methods of Chemotherapy (source: Chemocare, 2023)

LINK TO LEARNING

Chemotherapy Treatment

Access multimedia content (https://openstax.org/books/pharmacology/pages/8-2-chemotherapeutic-drugs)
This video describes the typical day and process of the treatment of a client receiving chemotherapy.

Phases of Chemotherapy

There are three phases of chemotherapy, beginning with induction. This phase is also known as first-line, front-line, or primary therapy. During this phase, the goal is to induce a remission. For most tumors, this may be the only phase required. For hematological cancers, clients may undergo a second phase, called consolidation, intensification, or post-remission therapy. This phase is used after a remission has been achieved, with a goal of eradicating any remaining cancer cells. The third phase, the maintenance phase, may be used either after induction or after consolidation. In this phase, a maintenance dose of chemotherapy is given to prevent reoccurrence of cancer. This phase is the longest phase and may last for several years.

Routes of Chemotherapy Administration

Chemotherapy may be administered by different routes depending on the purpose and toxicities of each individual drug. These different routes include oral, intravenous, subcutaneous, intramuscular, intracavitary, topically, and intrathecally. Intracavitary administration involves the infusion of a chemotherapeutic agent into a body cavity such as the bladder or abdomen. Intrathecal administration involves instilling chemotherapy into the spinal column or intracranially to treat cancers in the central nervous system. For drugs that are **vesicants**, which have the ability to cause necrosis if they **extravasate**, the intravenous route must be used. When a vesicant drug is being administered, slow administration in a rate/minute modality and vigilant assessment of the intravenous infusion site must be performed. Maintaining patency of the administration site is paramount to preventing tissue injury (see Figure 8.3).

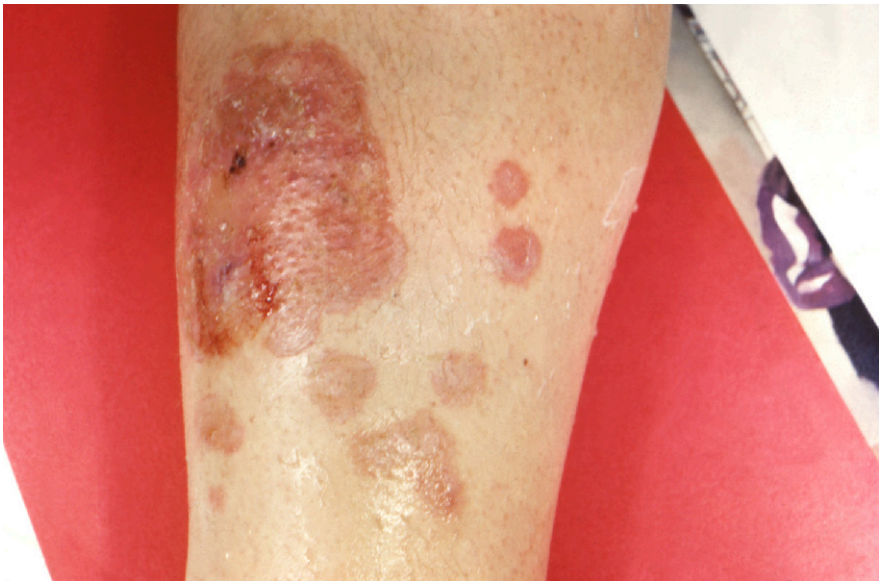


FIGURE 8.3 Vesicants can cause severe damage that can take months to heal. (credit: "This image depicted a view of the volar surface of a patient's right forearm, highlighting a number of erythematous, well-circumscribed lesions, which had resulted from an infection known as tinea corporis, more commonly referred to as ringworm" by Dr. Lucille K. Georg/Centers for Disease Control and Prevention, Public Domain)

CLINICAL TIP

Administering Vesicant Drugs

When administering a vesicant drug, the nurse should use extreme caution. If, for any reason, the nurse feels that an intravenous site could be compromised, the infusion should be immediately stopped and a new access obtained. Should an actual extravasation occur, the health care provider should be notified and any applicable protocols should be followed.

Chemotherapy may be given by different routes, depending on the cancer location. When cancer develops in a body cavity or in the brain or spinal column, treatment may require the use of special routes of administration to overcome the blood-brain barrier or to increase effectiveness by placing drug therapy more directly at the tumor site. Table 8.2 describes the different methods of chemotherapy administration.

Method of Chemotherapy Administration	Description
Oral	Tablets, capsules, or liquids that are swallowed
Intravenous	Liquid preparations administered into a vein via peripheral or central catheters
Injection	Liquid preparations administered via intramuscular or subcutaneous injections
Intrathecal	Injected by syringe or catheter directly into the brain or spinal cord
Intraperitoneal	Injected or infused via catheter into the peritoneal cavity
Intracavitary	Injected or infused via catheter into a body cavity such as the bladder
Intraarterial	Injected directly into an artery flowing to tumor sites
Topical	Applied directly to the skin or tumor site

TABLE 8.2 **Routes of Chemotherapy Administration**

Types of Chemotherapy

There are many different classifications of chemotherapy drugs, many of which fall into one of two broad categories—cell-cycle specific and cell-cycle nonspecific therapies. Each cell goes through five phases of mitosis

before producing daughter cells (see Figure 8.4). Chemotherapy agents that cause cancer cell death in all phases of mitosis are referred to as cell-cycle nonspecific (CCNS), whereas those that are effective only in one phase of mitosis are called cell-cycle specific agents (CCS). In combination chemotherapy, both CCS and NCCS agents are used to eliminate cancer cells more completely.

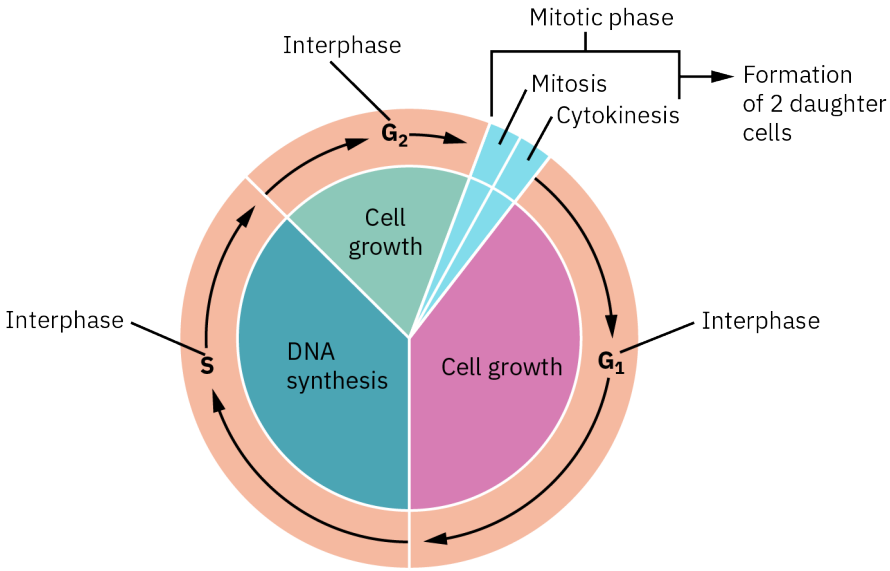


FIGURE 8.4 One phase of the cell cycle includes mitosis, when the cell divides. During this phase, the duplicated chromosomes are segregated and distributed into daughter nuclei. Following mitosis, the cytoplasm is usually divided as well by cytokinesis, resulting in two genetically identical daughter cells (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Side Effects of Chemotherapy

Side effects of chemotherapy vary from client to client and drug to drug. However, most chemotherapies have overlapping side effects. Each of these side effects must be managed appropriately to protect the client and promote positive outcomes. Nurses who care for clients receiving chemotherapy must possess excellent assessment skills to recognize and treat these side effects early.

Most chemotherapies work by interrupting DNA or RNA synthesis. These chemicals are most effective in eliminating cells that are most rapidly reproducing, with high mitotic rates. Unfortunately, chemotherapy cannot tell the difference in cells that are abnormally dividing versus normally rapidly dividing; therefore, the client may experience effects on normal cells as well. This includes hair, nails, skin, mucus membranes, the lining of the gastrointestinal system, and, most importantly, the stem cells within the bone marrow.

Major Side Effects

Most chemotherapy agents have major side effects in common. These include myelosuppression, alopecia, nausea and vomiting, skin or nail changes, and late-term effect, including **secondary cancers**. **Myelosuppression** is one of the most common effects of chemotherapy. This occurs as chemotherapy affects the stem cells in the bone marrow, resulting in decreased production of white blood cells, red blood cells, and platelets. Myelosuppression affecting red blood cells, white blood cells, and platelets all together is referred to as **pancytopenia**. Without proper support during this myelosuppression, clients may experience sepsis, bleeding, and hypoxemia, which may result in increased mortality rates. Frequent monitoring of the client's complete blood count is imperative. In some regimens, pancytopenia may happen very rapidly, in just a few days, while with other regimens, myelosuppression may not occur for 7–14 days or longer. The **nadir** period, or lowest point of myelosuppression, differs for each specific chemotherapy. Clients must be monitored closely after receiving myelosuppressive therapies for the nadir period, which predisposes clients to safety issues including infection, bleeding, impaired oxygenation, and falls. Protective measures must be instituted to prevent these from occurring, and the nurse must teach clients self-care principles (see Client Teaching Guidelines).

CLIENT TEACHING GUIDELINES

To prevent infection, the client receiving chemotherapy should:

- Bathe daily to reduce bacterial colonization.
- Cleanse their mouth after each meal and at bedtime.
- Cook eggs, meats, and seafood thoroughly to decrease the risk of foodborne illness.
- Use gloves when gardening to protect hands from direct contact with soil, which can contain bacteria and mold.
- Increase dietary fluids and fiber.
- Notify their health care provider for a temperature greater than 100.4°F (38°C), productive cough, diarrhea, or urinary burning, urgency, or frequency.

To prevent infection, the client receiving chemotherapy *should not:*

- Eat raw fruits and vegetables to decrease the risk of developing a foodborne illness.
- Eat wild game such as deer, rabbits, and pheasants to decrease the risk of ingesting contaminated meat.
- Clean cat litter boxes to decrease the risk of contact with bacteria or parasites.

Neutropenia, **leukopenia**, and **granulocytopenia** occur when the white cell indices (**neutrophils**, **leukocytes**, **granulocytes**) are decreased. This is typically defined as having an absolute neutrophil count less than 1.5 cells/mcL. When this occurs, the client may be prescribed prophylactic antibiotic therapy that may include broad-spectrum gram-positive, broad-spectrum gram-negative, and/or antifungal agents to assist in preventing sepsis. (See Anti-infective Drugs.) Clients with neutropenia present a fragile and complicated situation, especially in regard to nursing care and assessments. It is common for severely neutropenic clients to acquire infections, and even sepsis, with few clinical symptoms. Vigilant nursing assessment is a priority in preventing negative client outcomes. With low white blood cell counts, normal immune responses to infection may be absent. For example, a client who has developed a local infection at a central venous access site would normally display warmth, redness, and edema at the site. However, that same client, when experiencing neutropenia, would not exhibit these symptoms. During this time of decreased immunity, clients may also be treated with biologic colony stimulating agents such as filgrastim or pegfilgrastim. These drugs stimulate increases in stem cell production of white blood cells, accelerating a client's recovery from white blood cell destruction.

CLINICAL TIP

Febrile Neutropenia

Febrile neutropenia occurs when a client has an absolute neutrophil count that is less than 1.5 per microliter, accompanied by a body temperature above 100.4°F. When it occurs, febrile neutropenia should become first priority for assessment and intervention. The health care provider should be called immediately. Typically, blood cultures will be obtained, and the client will begin empiric broad-spectrum antibiotics. Failure to recognize and treat febrile neutropenia may result in life-threatening sepsis.

Thrombocytopenia, another result of myelosuppression, results in increased risk of bleeding as the number of circulating platelets (**thrombocytes**) decreases. Thrombocytopenia may cause gastrointestinal hemorrhage, intracerebral bleeding, and other sites of bleeding such as gum and scleral hemorrhages. Platelet counts less than 50,000 per microliter require special precautions; below 20,000, the bleeding risk greatly increases, and the client may require platelet transfusions.

CLIENT TEACHING GUIDELINES

To prevent bleeding, the client being treated for thrombocytopenia should:

- Use tooth sponges for oral care to decrease the risk of bleeding secondary to brushing. Avoid alcohol-

based mouthwash, which can dry the mouth and increase the risk of bleeding.
- Increase dietary fluids and fiber.
- Use stool softeners and fiber laxatives to produce regular, soft bowel movements.

To prevent bleeding, the client being treated for thrombocytopenia *should not:*

- Participate in contact sports or other activities that could cause bleeding.

Erythrocytopenia (anemia), a decrease in the production of red blood cells (**erythrocytes**), is another result of myelosuppression. Red blood cells function to carry oxygen to tissues, remove carbon dioxide from tissues, and provide volume within the intravascular space. When red blood cell counts decrease, clients may become hypoxemic when there are not enough red blood cells to transport oxygen. This results in fatigue and shortness of breath. Hypovolemia also occurs, in which decreased numbers of circulating red blood cells cause lowered vascular pressure. Clients may then experience orthostatic hypotension, dizziness, and disequilibrium. Clients may require transfusions of packed red blood cells, hydration with isotonic intravenous fluids, and oxygen. To decrease the occurrence of erythrocytopenia, clients may be given biologic colony stimulators to increase red blood cell production. These include epoetin alfa and darbepoetin.

CLIENT TEACHING GUIDELINES

To promote oxygenation, the client with anemia (erythrocytopenia) should:

- Schedule activities around periods of rest.
- Notify the health care provider if shortness of breath increases or does not resolve with rest.
- Sit on the side of the bed or chair for a few minutes before rising.

To promote oxygenation, the client with anemia (erythrocytopenia) *should not:*

- Perform tasks or engage in activities that cause shortness of breath.

Alopecia, or hair loss, is a side effect of some chemotherapies. Drugs such as doxorubicin damage hair follicles, which results in partial or complete hair loss. While this is not usually permanent, it will last throughout the duration of the treatments. Although this is not harmful for the client physically, it may be very difficult for a client emotionally and socially. Hair loss ultimately affects body image and self-esteem and may cause others to be uncomfortable around the client. Regrowth of hair usually begins within 6 months after treatments have finished (American Cancer Society, 2021).

Skin and nail changes may occur with administration of some types of cancer treatments. Skin rashes (erythema) or peeling of the skin on the hands and feet may occur. Hyperpigmentation of the skin and nail beds may develop as well. Tactile effects may cause neuropathic pain or increased sensitivity to cold. Nails may break, crack, or fall off. The nurse must provide care to prevent the development of infection should the nails or skin become broken.

Chemotherapy-associated nausea and vomiting is another common side effect and can vary from drug to drug and client to client. Risk factors for chemotherapy-induced nausea and vomiting include female sex, clients who experienced nausea and vomiting during pregnancy, age less than 50 years, and incidence of nausea and vomiting with previous chemotherapy treatments. Dehydration and electrolyte imbalances are also associated with increased nausea and vomiting. While there is pharmacological support for nausea and vomiting, some chemotherapeutic agents continue to cause significant negative effects. Nausea and vomiting may occur as anticipatory, beginning before a treatment begins, or during or soon after a treatment. Some agents like cisplatin may cause delayed nausea and vomiting, defined as occurring more than 24 hours after administration. This may last 5 days or more. Management of chemotherapy-induced nausea and vomiting includes efforts to maintain client comfort, adequate hydration, and electrolyte balance. Antiemetics such as ondansetron and aprepitant may be given before, during, and after treatment. Nutritional support to help maintain adequate intake of required nutrients and prevent chemotherapy-related cachexia (“wasting syndrome”) accompanies the management of nausea and vomiting.

For clients undergoing chemotherapy, another complication involves long-term effects. Most chemotherapy

treatments effectively begin both therapeutic and untoward effects as soon as they are administered. The acute effects may last throughout the treatment period and for a few months afterward. However, the cumulative effects of repeated cycles of treatment often result in effects that persist and even worsen over many years. Long-term effects typically involve decreased pulmonary and cardiac function, but other effects such as infertility may be seen.

In addition to monitoring for late-term effects of chemotherapies, clients must be evaluated for recurrence of disease and for development of secondary cancers. Recurrence of a tumor happens when cells of the original cancer return and begin growing despite treatment modalities. Secondary cancers differ from recurrent cancer in that these tumors develop in different tissues than the original cancer. Chemotherapeutic agents, unfortunately, are carcinogens. Receiving chemotherapeutic agents for cancer treatment places a client at risk of developing other types of cancers known as secondary cancers. For cancer survivors, follow-up care includes continued surveillance to assess for these effects.

Alkylating Drugs

Alkylating agents are among the oldest group of chemotherapies. They were developed after World War I when it was noted that these substances, when used as weapons, caused myelosuppression. Upon this discovery, they were developed into chemotherapeutic agents. In general, the medications in this class kill cancer cells by cross-linking DNA, which which prevents cell division in a manner that can lead to toxicity within the cell or unbalanced growth, both of which can cause cell death. These agents work most effectively on slower-growing tumors with a slowed mitotic rate. Alkylating agents are separated into several different subclasses. Some of these medications are dosed based on the client's weight, and others are administered based on the client's body surface area (BSA), which is determined using a formula using the client's height and weight (mg/m^2).

Subclass 1: Nitrogen Mustards

In use today are five alkylating agents that are classified as nitrogen mustards. These include mechlorethamine, melphalan, chlorambucil, ifosfamide, and cyclophosphamide. Cyclophosphamide is the most widely used nitrogen mustard and can be found in the regimens for many different cancers. Cyclophosphamide and ifosfamide pose the risk of **hemorrhagic cystitis**, usually when high-dose therapy is used. To prevent this, a rescue agent, or uroprotectant, is given to prevent bladder irritation. **Mesna** is the rescue agent used with these drugs for supportive interventions to prevent bladder complications.

Subclass 2: Nitrosoureas

Nitrosoureas are classified as alkylating agents, yet these have an advantage that nitrogen mustards do not: they cross the blood–brain barrier. This characteristic allows these drugs to pass into the brain, treating cancers like glioblastomas and other brain tumors. Carmustine is a more commonly used intravenous nitrosourea. Lomustine, which is similar to carmustine, is administered via oral routes.

Subclass 3: Alkyl Sulfonates

Alkyl sulfonates such as busulfan are administered as an intravenous (IV) infusion rather than IV push. These are very potent drugs, used to treat chronic leukemia, and they have severe adverse effects. These include myelosuppression, stomatitis, nausea, vomiting, diarrhea, and electrolyte imbalances including hypomagnesemia and hypokalemia. Busulfan requires very close pharmacokinetic monitoring and dose alteration.

Chemotherapy, while it acts to target cell functions and reproduction, may cause widespread undesired damage to normal cells. For this reason, many chemotherapeutic agents have black box warnings. These warnings are used to emphasize the most serious and potentially damaging side effects of a drug or a class of drugs. Boxed warnings are set specifically to make clients and health care providers aware of very serious risks of using certain medications. With chemotherapeutics, there are multiple reasons that a boxed warning may be issued. However, the most common reasons include myelosuppression, teratogenicity, and hypersensitivity reactions. Prior to administering a chemotherapeutic drug, nurses should check for boxed warnings so that drugs may be administered safely and clients may be educated regarding these warnings.

Table 8.3 lists common alkylating agents and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Nitrogen Mustards	
Cyclophosphamide (Cytoxan)	*Oral:* 1–5 mg/kg once daily. *Intravenous (IV) (monotherapy):* 40–50 mg/kg given in divided doses over 2–3 days, or 10–15 mg/kg given every 7–10 days. *IV (combination therapy):* 3–5 mg/kg given twice weekly. *Note:* Doses may be reported in grams versus milligrams.
Chlorambucil (Lukeran)	0.1–0.2 mg/kg orally once daily for 3–6 weeks.
Nitrosoureas	
Carmustine (BCNU)	150–200 mg/m^2 IV every 6 weeks administered as a single dose or divided injections on 2 successive days.
Lomustine (CCNU)	130 mg/m^2 orally every 6 weeks.
Alkyl Sulfonates	
Busulfan (Busulfex)	*Clients >12 kg:* 0.8 mg/kg IV as a single treatment, every 6 hours for 16 doses.
Alkylating-Like Drugs	
Cisplatin	*Advanced testicular cancer:* 20 mg/m^2 IV daily for 5 days. *Advanced ovarian cancer:* 75–100 mg/m^2 IV once every 3–4 weeks. *Advanced bladder cancer:* 50–70 mg/m^2 IV once every 3–4 weeks.
Carboplatin (Paraplatin)	300 mg/m^2 IV (combination therapy) or 360 mg/m^2 (monotherapy) every 4 weeks.
Oxaliplatin (Eloxatin)	85 mg/m^2 IV every 2 weeks.

TABLE 8.3 **Drug Emphasis Table: Alkylating Agents** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Alkylating agents are some of the most toxic chemotherapies used in cancer treatment. One benefit of these toxicities is that drugs like busulfan can be used to eradicate bone-marrow production prior to stem-cell and bone-marrow transplants. This reduces recurrence of the primary disease after transplant. However, alkylating agents are known for the negative effects associated with administration of these drugs. Short-term side effects include myelosuppression, which usually occurs 6–10 days after administration, with recovery after 14–21 days. Myelosuppression resulting in neutropenia can result in severe infections and sepsis. **Mucositis**, nausea, and vomiting are side effects that affect the client's overall nutritional status. Neurotoxicity and alopecia are also short-term side effects. Long-term (delayed) effects of alkylating agents include pulmonary fibrosis, infertility, and secondary malignancies (Amjad & Kasi, 2020). These long-term effects may occur months after treatment or may develop many years later.

Table 8.4 is a drug prototype table for alkylating agents featuring cyclophosphamide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Alkylating agent–nitrogen mustard Cell cycle nonspecific **Mechanism of Action** Causes crosslinking of DNA during mitosis to cause nucleic acid chain breakage resulting in cell destruction	**Drug Dosage** *Oral:* 1–5 mg/kg once daily. *Intravenous (IV) (monotherapy):* 40–50 mg/kg given in divided doses over 2–3 days, or 10–15 mg/kg given every 7–10 days. *IV (combination therapy):* 3–5 mg/kg given twice weekly. *Note:* Doses may be reported in grams versus milligrams.
Indications Lymphomas Multiple myeloma Leukemia Ovarian and breast cancers **Therapeutic Effects** Reduction of cancer cells	**Drug Interactions** Protease inhibitors Angiotensin-converting enzyme (ACE) inhibitors Thiazide diuretics Zidovudine Amiodarone
Adverse Effects Myelosuppression Sepsis Nephrotoxicity Pulmonary toxicity Cardiotoxicity Infertility Hyponatremia	**Contraindications** Myelosuppression Urinary outflow obstruction Caution: Monitor for hemorrhagic cystitis Mesna may be used in high-dose therapy to prevent bladder irritation

TABLE 8.4 **Drug Prototype Table: Cyclophosphamide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking alkylating agents:

- Assess client overall well-being prior to chemotherapy administration, including vital signs, hydration status, and weight.
- Review laboratory values thoroughly, including complete blood counts, electrolyte profiles, serum creatinine, and liver enzymes.
- Observe clients for adverse effects before, during, and after treatment.
- Ensure patency of intravenous access sites and monitor these frequently during drug administration.
- Adhere to proper handling and administration procedures when administering chemotherapies.
- Be prepared to manage extravasation and follow spill protocols.
- Become familiar with the drug's black box warnings.
- Recognize and manage emergent situations such as hypersensitivity reactions, bleeding, and sepsis.
- Assess for and provide supportive therapies as needed.
- Provide for educational, spiritual, and psychosocial needs of the client and caregivers.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an alkylating drug should:

- Report the following signs and symptoms to the health care provider: fever, chills, productive cough, urinary symptoms, hematuria (cyclophosphamide), changes in hearing (cisplatin).
- Remain well hydrated. Report side effects including nausea and vomiting and mucositis.
- Know how to care for long-term intravenous access at home.

- Understand the need for frequent follow-up and laboratory tests.
- Know which drug/food interactions to avoid.
- Monitor for and report any long-term effects of the chemotherapy.
- Follow up with all recommended health screenings.
- Report any concerning signs and symptoms to their health care provider.

The client taking an alkylating drug *should not:*

- Be around others who are ill or who have received live vaccines within 3 months.
- Garden without the use of gloves to protect their hands from the risk of bacterial contamination.
- Clean feline litter boxes to decrease the risk of exposure to bacteria or parasites.
- Take vaccines without their health care provider's approval.
- Consume uncooked meats and wild game such as deer, rabbits, and pheasants.
- Begin taking new supplements or medications without consulting their health care provider.
- Become pregnant.

FDA BLACK BOX WARNING

Various Alkylating Agents

Busulfan injection causes severe and prolonged myelosuppression at the recommended dosage.

Carboplatin causes severe bone marrow suppression, resulting in bleeding, infection, and anemia. Anaphylactic-like reactions to carboplatin may occur within minutes of administration.

Carmustine causes bone marrow suppression, which may contribute to bleeding and overwhelming infection. In cumulative doses above 1400 mg/m^2, pulmonary toxicity is a significant risk.

Chlorambucil causes severe bone marrow suppression and infertility and is carcinogenic, mutagenic, and teratogenic.

Cisplatin causes severe renal toxicity that is dose related and cumulative. Peripheral neuropathy occurs and is cumulative with repeat courses. Cisplatin causes severe nausea and vomiting. Bone marrow suppression may be severe, requiring interruption of therapy.

Lomustine causes severe, dose-related, delayed, and cumulative myelosuppression, occurring 4–6 weeks after administration. Overdose is fatal. Only 1 dose should be dispensed with each prescription.

Oxaliplatin may cause anaphylactic-like reactions that may occur within minutes of administration.

Antimetabolites

Antimetabolite chemotherapies are a group of drugs that prevent cancer cell growth by imitating metabolites, which are substances necessary for tumor cell growth. Cancer cells use these substances, which, once inside the cell, prevent DNA replication. This results in cell death. Within this class, there are three types of metabolites that are inhibited: purines, pyrimidines, and folic acid. Each drug in this class specifically targets replacement of one of these substances. The most common drugs within this class are fluorouracil, fludarabine, gemcitabine, and methotrexate. Common side effects include nausea and vomiting, diarrhea, anorexia, stomatitis, alopecia, and myelosuppression. Antimetabolites are useful in treating leukemias, lymphomas, and cancers of the gastrointestinal and biliary tracts.

Table 8.5 lists common antimetabolite agents and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Folate Antimetabolites	
Methotrexate (Trexall)	*Intrathecal:* 6–15 mg/m^2 age-based dose; frequency depends on regimen. *IV:* 10 mg/m^2 up to 12,000 mg/m^2 at varying frequencies depending on the diagnosis and treatment regimen.
Pemetrexed (Alimta)	500 mg/m^2 IV every 21 days.
Pyrimidine Antimetabolites	
5-Fluorouracil (5-FU)	*Colon/rectal adenocarcinoma:* 400 mg/m^2 IV bolus followed by 2400–3000 mg/m^2 continuous infusion over 46 hours every 2 weeks. *Pancreatic adenocarcinoma:* 400 mg/m^2 IV bolus followed by 2400 mg/m^2 continuous infusion over 46 hours every 2 weeks. *Breast adenocarcinoma:* 500–600 mg/m^2 IV days 1 and 8 every 28 days for 6 cycles. *Gastric adenocarcinoma:* 200–1000 mg/m^2 IV over 24 hours at varying frequencies depending on regimen.
Capecitabine (Xeloda)	1250 mg/m^2 orally twice daily for 2 weeks followed by a 1-week rest period.
Cytarabine (Ara-C)	*IV:* 100 mg/m^2 daily as a single treatment over 7 days. *Intrathecal:* 5–75 mg/m^2 once every 4 days.
Purine Antimetabolites	
Mercaptopurine (Purixan)	1.5–2.5 mg/kg orally once daily.
Thioguanine (Tabloid)	2–3 mg/kg orally daily.
Gemcitabine (Gemzar)	1000 mg/m^2 IV on days 1 and 8 of a 21-day cycle.
Fludarabine (Fludara)	25 mg/m^2 IV daily for 5 days, every 28 days.

TABLE 8.5 **Drug Emphasis Table: Antimetabolite Agents** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Antimetabolites are associated with many adverse effects. Folate antimetabolites are associated with myelosuppression, mucositis, hepatotoxicity, nephrotoxicity, and cutaneous reactions. Pyrimidine antimetabolites cause mucositis and myelosuppression as well but are also associated with dose-limiting hand-foot syndrome and diarrhea. Contraindications for fluorouracil include clients with dihydropyridine dehydrogenase (DPD) deficiency, which may result in toxic levels of fluorouracil. This can lead to cardiac dysfunction, colitis, neutropenia, and encephalopathy. Uridine triacetate is used to treat toxicity in these clients. Cytarabine is associated with inflammation of the conjunctiva. Corticosteroid eye drops are used prophylactically to prevent this. Purine antimetabolites, in addition to causing myelosuppression, also decrease the CD4 lymphocyte count, resulting in immunosuppression and risk of opportunistic infections (Amjad & Kasi, 2020).

Table 8.6 is a drug prototype table for antimetabolites featuring fluorouracil. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antimetabolite (pyrimidine antagonist) **Mechanism of Action** Antagonizes metabolites necessary for cell growth, results in apoptosis (cell death) of cancerous cells	**Drug Dosage** *Colon/rectal adenocarcinoma:* 400 mg/m^2 IV bolus followed by 2400–3000 mg/m^2 continuous infusion over 46 hours every 2 weeks. *Pancreatic adenocarcinoma:* 400 mg/m^2 IV bolus followed by 2400 mg/m^2 continuous infusion over 46 hours every 2 weeks. *Breast adenocarcinoma:* 500–600 mg/m^2 IV days 1 and 8 every 28 days for 6 cycles. *Gastric adenocarcinoma:* 200–1000 mg/m^2 IV over 24 hours at varying frequencies depending on regimen.
Indications Breast, colon, pancreatic, and gastric cancers **Therapeutic Effects** Prevents DNA synthesis to cause tumor cell death	**Drug Interactions** Warfarin
Adverse Effects Mucositis Diarrhea Hand-foot syndrome Myelosuppression Neurotoxicity Gastrointestinal ulcers	**Contraindications** Hypersensitivity Decreased dipyridine dehydrogenase Caution: Increases international normalized ratio (INR) when administered to clients receiving warfarin

TABLE 8.6 **Drug Prototype Table: Fluorouracil** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antimetabolite agents:

- Assess client overall well-being prior to chemotherapy administration, including vital signs, hydration status, oral mucosa, skin, eyes (cytarabine), and weight.
- Review laboratory values thoroughly, including complete blood counts, electrolyte profiles, serum creatinine, and liver enzymes. Observe clients for adverse effects before, during, and after treatment.
- Ensure patency of intravenous access sites and monitor these frequently during drug administration.
- Adhere to proper handling and administration procedures when administering chemotherapies.
- Be prepared to manage extravasation and spill protocols.
- Be aware of drugs' boxed warnings.
- Recognize and manage emergent situations such as hypersensitivity reactions, bleeding, and sepsis.
- Assess for and provide supportive therapies as needed.
- Provide for educational, spiritual, and psychosocial needs of the client and caregivers.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antimetabolite agent should:

- Report the following signs and symptoms to the health care provider: fever, chills, productive cough, urinary symptoms, hematuria, eye irritation (cytarabine), and mouth ulcers (fluorouracil).
- Remain well hydrated.
- Report side effects including nausea and vomiting and mucositis.
- Know how to care for long-term intravenous accesses at home.
- Understand the need for frequent follow-up and laboratory tests.
- Know which drug/food interactions to avoid.

- Monitor and report any long-term effects.
- Follow up with recommended screenings for early identification of any secondary malignancies.

The client taking an antimetabolite *should not:*

- Be around others who are ill or who have received live vaccines within 3 months.
- Garden without the use of gloves to decrease the risk of exposure to mold and bacteria.
- Clean feline litter boxes to minimize bacteria or parasite exposure.
- Take vaccines without consulting with their health care provider.
- Consume uncooked meats and wild game such as deer, rabbits, and pheasants.
- Begin taking new supplements or medications without consulting their health care provider.
- Become pregnant.

FDA BLACK BOX WARNING

Antimetabolites

Methotrexate causes embryo-fetal toxicity, hypersensitivity reactions, benzyl alcohol toxicity, and other serious adverse reactions.

Capecitabine causes increased risk for bleeding when administered with coumarins such as warfarin.

Fludarabine causes severe central nervous system toxicity, including blindness, coma, seizures, and death. Autoimmune syndromes including hemolytic anemia, thrombocytopenia, and hemophilia may occur with fludarabine administration. Concomitant use of deoxycoformycin (pentostatin) may cause fatal pulmonary toxicity.

Anthracyclines/Antitumor Antibiotics

Anthracyclines are some of the most potent chemotherapies on the market today. These drugs are very strong vesicants that cause severe necrosis when extravasated. Three major drugs in this class are daunorubicin, doxorubicin, and epirubicin. These drugs cause cell death by preventing DNA replication. They do this by inhibiting topoisomerase, leaving DNA strands unable to unwind and replicate. The major side effects of anthracyclines are myelosuppression, nausea and vomiting, alopecia, skin and nail hyperpigmentation, and, most notably, cardiotoxicity. Many drugs in this class are red in color and can resultingly cause urine and other body fluids to turn red/orange. This is a benign side effect but is usually discussed with clients to avoid any panic. These drugs are assigned maximum lifetime dose limits to aid in preventing debilitating chemotherapy-induced heart failure. Additionally, clients must have a left ventricular ejection fraction of at least 55% to receive these drugs. Table 8.7 lists common anthracyclines/antitumor antibiotics and typical routes and dosing for adult clients.

Drug	Drug Routes and Dosages
Anthracyclines/Antitumor Antibiotics	
Daunorubicin (Cerubidine)	25–45 mg/m^2 IV; frequency depends on cancer type and other agents administered in combination (550 mg/m^2 maximum lifetime limit due to cardiac toxicity).
Doxorubicin (Adriamycin, Doxil)	60–75 mg/m^2 IV every 21 days (550 mg/m^2 maximum lifetime limit due to cardiac toxicity).
Epirubicin (Ellence)	*IV:* 100–120 mg/m^2 frequency depends on prescribed regimen (720 mg/m^2 maximum lifetime limit due to cardiac toxicity).
Other Anthracyclines	
Bleomycin (Blenoxane)	0.25–0.5 units/kg (10–20 units/m^2) given IV, intamuscularly, or subcutaneously weekly or twice weekly. (Drug may be discontinued if pulmonary toxicity occurs.)

TABLE 8.7 **Drug Prototype Table: Anthracyclines/Antitumor Antibiotics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Drug Routes and Dosages
Dactinomycin (Cosmegen)	12–1250 mcg/m^2 IV; frequency depends on cancer type.
Mitomycin (Mutamycin)	20 mg/m^2 IV at 6–8 week intervals.

TABLE 8.7 **Drug Prototype Table: Anthracyclines/Antitumor Antibiotics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Anthracyclines and antitumor antibiotics are associated with very serious adverse effects. In general, the drugs cause significant myelosuppression, alopecia, and nausea and vomiting. Doxorubicin and daunorubicin are associated with both short- and long-term cardiotoxicity. These drugs are contraindicated in clients with preexisting cardiac disease when the left ventricular ejection fraction is less than 55%. Clients receiving doxorubicin are also limited to a lifetime cumulative dose of 550 mg/m^2. Bleomycin administration requires vigilant monitoring for cumulative **pulmonary toxicity** and **fibrosis**. Doxorubicin and daunorubicin are vesicant drugs that cause severe necrosis if extravasation into tissues occurs.

Table 8.8 is a drug prototype table for anthracycline agents featuring doxorubicin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anthracycline/antitumor antibiotic **Mechanism of Action** Inhibits topoisomerase to prevent DNA replication	**Drug Dosage** 60–75 mg/m^2 IV every 21 days (550 mg/m^2 maximum lifetime limit due to cardiac toxicity).
Indications Breast, bronchogenic, and thyroid cancers Leukemia Lymphoma Sarcoma Wilms tumor **Therapeutic Effects** Prevents DNA synthesis to cause tumor cell death	**Drug Interactions** Paclitaxel Trastuzumab 6-mercaptopurine Dexrazoxane (may be used as a cardioprotective agent in certain populations or upon extravasation)
Adverse Effects Cardiotoxicity Myelosuppression Alopecia Hyperpigmentation of skin and nails Stomatitis	**Contraindications** Hypersensitivity Myelosuppression Decreased cardiac function Caution: 550 mg/m^2 maximum lifetime limit Client must have ejection fraction of at least 55% to receive doxorubicin Severe necrosis with extravasation

TABLE 8.8 **Drug Prototype Table: Doxorubicin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking anthracyclines/antitumor antibiotic agents:

- Assess client overall well-being prior to chemotherapy administration including vital signs, hydration status, oral mucosa, skin, and weight.
- Review laboratory values thoroughly, including complete blood counts, electrolyte profiles, serum creatinine, liver enzymes, and left ventricular ejection fraction and pulmonary function tests (bleomycin).
- Carefully record cumulative doses when lifetime limits are necessary.

- Observe clients for adverse effects before, during, and after treatment.
- Ensure patency of intravenous access sites and monitor these frequently during drug administration.
- Adhere to proper handling and administration procedures when administering chemotherapies.
- Be prepared to manage extravasation and follow spill protocols.
- Be aware of the drug's black box warnings.
- Recognize and manage emergent situations such as hypersensitivity reactions, bleeding, and sepsis.
- Assess for and provide supportive therapies as needed.
- Provide for educational, spiritual, and psychosocial needs of the client and caregivers.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an anthracycline/antitumor antibiotic agent should:

- Know signs and symptoms to report to the health care provider, including fever, chills, productive cough, urinary symptoms, hematuria, palpitations, chest pain, shortness of breath (doxorubicin, daunorubicin, epirubicin), pulmonary pain, and breathing difficulties (bleomycin).
- Remain well-hydrated.
- Report side effects including nausea and vomiting and mucositis.
- Know how to care for long-term intravenous accesses at home.
- Understand the need for frequent follow-up and laboratory tests.
- Know which drug/food interactions to avoid.
- Follow up with screenings for long-term effects and secondary malignancies.

The client taking an anthracycline and antitumor antibiotic agent *should not:*

- Be around others who are ill or who have received live vaccines within 3 months.
- Garden without the use of gloves to protect hands from direct contact with bacteria and mold present in the soil.
- Clean feline litter boxes to reduce risk of contact with bacteria and parasites.
- Take vaccines without prior approval of their health care provider.
- Consume uncooked meats and wild game such as deer, rabbits, and pheasants.
- Begin taking new supplements or medications without consulting their health care provider.
- Become pregnant.

FDA BLACK BOX WARNING

Doxorubicin and Epirubicin

Potentially fatal congestive heart failure can occur during or years after therapy. The probability is based on the total cumulative doses received.

Secondary acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) has been reported in clients taking these medications.

Plant Alkaloids

Several chemotherapies are derived from plants and are considered **plant alkaloids**. Vinca alkaloids are the most common plant alkaloids. Vincristine, vinblastine, and etoposide (VP-16) are all plant alkaloids that cause misalignment of chromosomes in cancer cells, resulting in apoptosis, or cell death. These are useful in treating lymphomas, leukemias, Kaposi sarcoma, squamous cell carcinomas, lung cancer, and bladder cancer. Side effects include myelosuppression, mouth sores, nausea, vomiting, and fatigue. The most significant adverse effects involve the nervous system. Because plant alkaloids decrease nerve function, these substances can cause hearing loss, neuropathies, and severe constipation that may develop into a paralytic ileus. Neurologic symptoms may

necessitate discontinuance of therapy. Vinca alkaloids are often part of regimens that also require intrathecal administration. However, close attention and safety measures (i.e., drug is always compounded in an IV bag for infusion) must be in place to ensure these are *never* administered via the intrathecal route. The drugs are fatal if administered intrathecally.

Table 8.9 lists common plant alkaloids and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Vincristine (Oncovin)	1.4 mg/m^2 IV weekly.
Vinblastine (Velban)	3.7 mg/m^2 IV initial dose; subsequent doses up to 18.5 mg/m^2 administered weekly.
Etoposide (Vepesid, VP-16)	35–100 mg/m^2 IV; frequency depends on cancer type and other agents administered.

TABLE 8.9 **Drug Emphasis Table: Plant Alkaloids** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Peripheral neuropathy is a common but serious adverse effect of plant alkaloids. Both motor and sensory functions are affected, and neuropathy can be severe enough to result in paralytic ileus. Myelosuppression is another adverse effect caused by plant alkaloids. These drugs are classified as irritants, which may cause significant irritation to the skin should extravasation occur.

Table 8.10 is a drug prototype table for plant alkaloids featuring vincristine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Plant alkaloid **Mechanism of Action** Causes chromosomal link errors, results in apoptosis of cancerous cells	**Drug Dosage** 1.4 mg/m^2 IV weekly.
Indications Lymphoma Leukemia Kaposi sarcoma Squamous cell carcinoma Lung cancer Bladder cancer **Therapeutic Effects** Prevents DNA synthesis to cause tumor cell death	**Drug Interactions** Anticonvulsants Amiodarone Carvedilol Erythromycin Fluconazole Rifampin Warfarin **Food Interactions** Grapefruit
Adverse Effects Neuropathy Severe constipation Paralytic ileus Urinary retention Hearing loss Alopecia	**Contraindications** Hypersensitivity Charcot-Marie-Tooth disease Caution: For intravenous administration only Fatal if administered intrathecally Causes severe irritation with extravasation

TABLE 8.10 **Drug Prototype Table: Vincristine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking plant alkaloid agents:

- Assess client overall well-being prior to chemotherapy administration including vital signs, hydration status, oral mucosa, skin, weight, bowel function, and signs of neuropathy.
- Review laboratory values thoroughly, including complete blood counts, electrolyte profiles, serum creatinine, and liver enzymes.
- Observe clients for adverse effects before, during, and after treatment.
- Inspect drug preparation to ensure that these drugs are properly mixed and prepared as intravenous infusions. Do not administer these medications directly to the client using a syringe. This will decrease the risk of having the medication erroneously administered intrathecally, which can be fatal. Ensure patency of intravenous access sites and monitor these frequently during drug administration.
- Adhere to proper handling and administration procedures when administering chemotherapies.
- Be prepared to manage extravasation and follow spill protocols.
- Be aware of the drug's black box warnings.
- Recognize and manage emergent situations such as hypersensitivity reactions, bleeding, and sepsis.
- Assess for and provide supportive therapies as needed.
- Provide for educational, spiritual, and psychosocial needs of the client and caregivers.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a plant alkaloid agent should:

- Report the following signs and symptoms to the health care provider: fever, chills, productive cough, urinary symptoms, hematuria, decreased bowel elimination or constipation, hearing loss, and peripheral neuropathy.
- Remain well hydrated and use stool softeners and laxatives when needed.
- Report side effects including nausea and vomiting, mucositis, and constipation.
- Learn how to care for long-term intravenous accesses at home.
- Understand the need for frequent follow-up and laboratory tests.
- Know which drug/food interactions to avoid.
- Understand the need for surveillance for long-term effects and secondary malignancies.

The client taking a plant alkaloid agent *should not:*

- Be around others who are ill or who have received live vaccines within 3 months.
- Garden without the use of gloves to avoid direct contact with potentially contaminated soil.
- Clean feline litter boxes to protect hands from contamination by bacteria or parasites.
- Take vaccines without consulting with their health care provider.
- Consume uncooked meats and wild game such as deer, rabbits, and pheasants.
- Begin taking new supplements or medications without consulting their health care provider.
- Become pregnant.

Taxanes

Taxanes are a group of chemotherapeutic agents that were developed from the bark of a yew tree. These are effective in the treatment of breast, ovarian, prostate, gastric, esophageal, pancreatic, and non-small cell lung cancers as well as Kaposi sarcoma. These agents are typically used in combination with other agents rather than as a monotherapy. Adverse reactions include, most notably, hypersensitivity reactions. For this reason, clients will be premedicated, usually with corticosteroids, but may also receive diphenhydramine and a histamine-2 receptor antagonist to prevent these reactions from occurring. Other adverse effects include hepatotoxicity, fluid retention, myelosuppression, alopecia, skin and nail changes, and nausea, vomiting, and diarrhea.

Table 8.11 lists common taxanes and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Docetaxel (Taxotere)	60–100 mg/m^2 IV every 3 weeks.
Paclitaxel (Taxol)	100–175 mg/m^2 IV every 3 weeks.

TABLE 8.11 **Drug Emphasis Table: Taxanes** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Taxanes are most known for the adverse effect of hypersensitivity reactions. A test dose and premedication with antihistamines and acetaminophen may be used prior administration. Myelosuppression may result in lowered levels of platelets and white blood cells. Taxanes are contraindicated in solid tumors with myelosuppression with neutrophil counts under 1500 cells/mm^3. Peripheral neuropathy is also commonly associated with taxanes, resulting in pain and limited movement. Fatigue and arthralgias are also seen with these drugs. Cardiovascular changes including hypotension, bradycardia, hypertension, and electrocardiogram (ECG, EKG) changes may be noted (DailyMed, *Paclitaxel*, 2023).

Table 8.12 is a drug prototype table for taxanes featuring paclitaxel. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Taxane **Mechanism of Action** Binds to microtubules to block spindle formation during mitosis, blocking cell division during the M phase of mitosis	**Drug Dosage** 100–175 mg/m^2 IV every 3 weeks.
Indications Breast, ovarian, and non-small cell lung cancers Kaposi sarcoma **Therapeutic Effects** Prevents tumor cell growth	**Drug Interactions** Midazolam Buspirone Statins Felodipine Protease inhibitors Repaglinide Rifampin
Adverse Effects Hypersensitivity reactions Myelosuppression ECG changes Peripheral neuropathy Arthralgia Nausea Vomiting Diarrhea Mucositis Alopecia Infusion site reactions	**Contraindications** Hypersensitivity Myelosuppression with neutrophil counts under 1500 µL Caution: May cause anaphylaxis due to the medication vehicle, not the drug itself Must premedicate

TABLE 8.12 **Drug Prototype Table: Paclitaxel** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking taxane agents:

- Assess client overall well-being prior to chemotherapy administration, including vital signs, hydration status, oral mucosa, skin, weight, cardiac function, and signs of neuropathy.
- Review laboratory values thoroughly, including complete blood counts, electrolyte profiles, serum creatinine,

and liver enzymes.
- Observe clients for adverse effects before, during, and after treatment.
- Ensure patency of intravenous access sites and monitor these frequently during drug administration.
- Adhere to proper handling and administration procedures when administering chemotherapies.
- Be prepared to manage extravasation and follow spill protocols.
- Be aware of the drug's black box warnings.
- Recognize and manage emergent situations such as hypersensitivity reactions, bleeding, and sepsis.
- Assess for and provide supportive therapies as needed.
- Provide for educational, spiritual, and psychosocial needs of the client and caregivers.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a taxane agent should:

- Recognize signs and symptoms to report to the health care provider: fever, chills, productive cough, urinary symptoms, hematuria, decreased bowel elimination or constipation, hearing loss, and peripheral neuropathy.
- Understand the importance of remaining well hydrated and use stool softeners and laxatives when needed.
- Learn how to manage side effects including nausea and vomiting, mucositis, and constipation.
- Understand how to care for long-term intravenous accesses at home.
- Understand the need for frequent follow-up and laboratory tests.
- Know which drug/food interactions to avoid.
- Understand the need for surveillance and follow-up for management of long-term effects and early identification of secondary malignancies.

The client taking a taxane agent *should not:*

- Be around others who are ill or who have received live vaccines within 3 months.
- Garden without the use of gloves to protect hands from exposure to bacteria and mold.
- Clean feline litter boxes to protect hands from direct contact with bacteria.
- Take vaccines without consulting with their health care provider.
- Consume uncooked meats and wild game such as deer, rabbits, and pheasants.
- Begin taking new supplements or medications without consulting with their health care provider.
- Become pregnant.

FDA BLACK BOX WARNING

Docetaxel

Docetaxel has been associated with fatalities among clients with abnormal liver function, who are receiving higher doses, with non-small cell carcinoma, or with a history of receiving platinum-based chemotherapy including cisplatin, carboplatin, and oxaliplatin.

Common Drugs Used as Supportive Therapies for Clients Receiving Chemotherapy

Because chemotherapy regimens are so complex, supportive care with other pharmacologic agents is usually required. Management of adverse effects is critical to safe and successful chemotherapy treatment. Myelosuppression and nausea and vomiting are most commonly managed with supportive therapies. Corticosteroids and biologic colony stimulating factors are frontline supportive therapies. Table 8.13 encompasses the most common supportive therapies that may be necessary when administering chemotherapy.

Classification/Drug	Routes and Dosages	Use
Corticosteroids		
Dexamethasone (Decadron)	*Oral:* 0.75–9 mg/day. *IV/intramuscular:* 0.5–9 mg/day.	Decreases nausea and vomiting. Used as premedication to reduce hypersensitivity reactions.
Antihistamines		
Diphenhydramine (Benadryl)	*Oral:* 25–50 mg every 4–6 hours as needed. *IV/intramuscular*: 10–50 mg up to 100 mg if required; 400 mg maximum daily dose.	Treats/prevents hypersensitivity reactions.
Loratadine (Allegra)	*Oral:* 10 mg 1 hour prior to chemotherapy initiation.	Prevents hypersensitivity reactions.
Colony Stimulating Factors		
Filgrastim (Neupogen)	5–10 mcg/kg/day administered as a single daily subcutaneous or IV injection or by continuous subcutaneous or IV infusion.	Stimulates bone marrow stem cells to produce increased neutrophil production. Prevents infection.
Pegfilgrastim (Neulasta)	6 mg/dose subcutaneously.	Stimulates bone marrow stem cells to produce increased neutrophil production. Prevents infection.
Epoetin alfa (Epogen)	150 units/kg subcutaneously 3 times weekly or 40,000 units/dose weekly; titrated based on hemoglobin response.	Stimulates bone marrow stem cells to produce increased erythocyte production. Prevents/treats anemia.

TABLE 8.13 **Most Common Supportive Therapies Used with Chemotherapy** (source: https://dailymed.nlm.nih.gov/dailymed/)

These supportive therapies can increase the client's quality of life as well as decrease risks associated with pancytopenia, such as sepsis and decreased oxygen-carrying capacity of the blood. The advent of biologic colony stimulating factors marked a significant decrease in sepsis-related deaths for clients receiving chemotherapy. Ondansetron, specifically, has greatly changed the way chemotherapy-related nausea and vomiting are treated. Traditional phenothiazines cause vein and tissue irritation as well as central nervous system depression, placing a client at risk for injury. Ondansetron does not affect central nervous system function, reducing the risk of falls and other injuries.

FDA BLACK BOX WARNING

Erythropoiesis-Stimulating Agents (ESAs)

Erythropoiesis-stimulating agents (ESAs) increase the risk of death, myocardial infarction, stroke, venous thromboembolism, and tumor progression or recurrence.

UNFOLDING CASE STUDY

Part A

Read the following clinical scenario to answer the questions that follow. This case will evolve throughout the chapter.

Guadalupe Himenez is a 32-year-old female client who presents to the oncology clinic for her first visit after recently

being diagnosed with breast cancer. She initially saw her gynecologist after detecting a lump in her left breast. Her provider ordered a mammogram and biopsy, which determined the mass was malignant, and a surgeon performed a lumpectomy to remove it. The surgeon has referred her to the oncologist to start chemotherapy. Prior to this, she has been in good health without any chronic medical conditions.

Social History
Tobacco use: None
Alcohol use: Occasionally drinks socially
Married with two children

Current Medications
None

Vital Signs		Physical Examination
Temperature:	98.2°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* S1, S2 noted • *Respiratory:* Clear bilaterally • *GI:* Abdomen soft, nontender, nondistended • *GU:* Reports normal urine output • *Neurological:* Within normal limits • *Integumentary:* Skin appropriate; healing surgical incision noted on the left breast; no signs of infection • *GYN:* History of two pregnancies with two living children
Blood pressure:	122/76 mm Hg	
Heart rate:	73 beats/min	
Height:	5'7"	
Weight:	174 lb	

TABLE 8.14

1. While completing the initial assessment, which of the following is a priority to assess?
   a. Social support
   b. Family history of cancer
   c. Date of last menstrual period
   d. Food preferences

2. After discussing all the treatment options, Guadalupe consents to starting chemotherapy. What type of treatment is this?
   a. Adjuvant therapy
   b. Neoadjuvant therapy
   c. Biologic therapy
   d. Salvage therapy

8.3 Hormonal Therapy

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 8.3.1 Identify the characteristics of hormonal therapy drugs used to treat cancer.
- 8.3.2 Explain the indications, actions, adverse reactions, and interactions of hormonal therapy drugs used to treat cancer.
- 8.3.3 Describe the nursing implications of hormonal therapy drugs used to treat cancer.
- 8.3.4 Explain the client education related to hormonal therapy drugs used to treat cancer.

Antiestrogen Medications

Antiestrogens, or estrogen antagonists, are a group of medications used to block estrogen receptors. By blocking these receptors, cancer cells that require estrogen for growth are no longer able to undergo mitosis and cannot cause tumor development. These drugs are classified as hormonal therapies, as they block the influence of the hormone estrogen. They are primarily used for breast cancer; however, antiestrogens are only effective in breast cancers that are hormone-receptor positive. Tamoxifen and fulvestrant are two commonly used antiestrogens used

for breast cancer. Tamoxifen is an oral medication that is given for approximately 5 years after breast cancer treatment. Fulvestrant, given intramuscularly, and elacestrant, a newer oral medication approved in 2023, are selective estrogen downregulators (SERD) that block estrogen receptors.

Aromatase Inhibitors

Aromatase inhibitors are another classification of **hormonal therapy** used to treat breast cancer in postmenopausal clients. Aromatase is an enzyme found in fatty tissue that converts hormones into estrogen. Aromatase inhibitors, including anastrozole and exemestane, stop the production of estrogen and thus the growth of estrogen receptor–positive tumors by blocking aromatase. These medications are taken daily as an oral tablet. Aromatase inhibitors may be prescribed for clients who are not good candidates for antiestrogens. Aromatase inhibitors may cause symptoms of menopause and muscle and joint pain, which may limit use if clients are not able to tolerate side effects. These drugs may also put clients at higher risk of osteoporosis (DailyMed, *Anastrozole*, 2023).

Antiandrogens

Antiandrogens, also known as androgen inhibitors or testosterone blockers, are hormonal therapies used to treat prostate cancer. These drugs block androgen receptors so that cancers that rely on testosterone and other hormones to grow cannot survive. These drugs may induce a reduction in masculine characteristics such as hair growth and erectile dysfunction. Drugs in this class include flutamide and bicalutamide. They are given by the oral route daily. Liver enzymes must be periodically evaluated during therapy, as these drugs are hepatotoxic.

Table 8.15 lists common hormonal therapies and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Antiestrogens	
Tamoxifen (Nolvadex)	20–40 mg/day orally for up to 5 years.
Fulvestrant (Faslodex)	500 mg intramuscularly divided into 2 injections, given initially on days 1, 15, and 29, and then monthly thereafter.
Aromatase Inhibitors	
Anastrozole (Arimadex)	1 mg/day orally.
Exemestane (Aromasin)	25 mg orally daily after a meal.
Antiandrogens	
Flutamide (Eulexin)	250 mg orally every 8 hours/750 mg daily.
Bicalutamide (Casodex)	50 mg/day orally.

TABLE 8.15 Drug Emphasis Table: Hormonal Therapies (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Tamoxifen citrate tablets are contraindicated in clients who require concomitant coumarin-type anticoagulant therapy or in clients with a history of deep-vein thrombosis or pulmonary embolus. Adverse effects of hormonal therapies include weight gain, fatigue, vaginal dryness, loss of interest in sex, hot flashes, osteoporosis, nausea, vomiting, and diarrhea. Male clients receiving hormonal treatment, such as for prostate cancer, may experience breast development and tenderness (DailyMed, *Tamoxifen*, 2022).

Table 8.16 is a drug prototype table for hormonal agents featuring tamoxifen. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antihormonal—antiestrogen **Mechanism of Action** Blocks estrogen receptors in estrogen receptor–positive tumors	**Drug Dosage** 20–40 mg/day orally for up to 5 years.
Indications Metastatic breast cancer **Therapeutic Effects** Prevents and inhibits growth of breast cancer that is stimulated by estrogens	**Drug Interactions** Erythromycin Cyclosporine Diltiazem Nifedipine Letrozole Aminoglutethimide **Food Interactions** None reported
Adverse Effects Amenorrhea Flushing, hot flashes Fluid retention Weight gain Nausea Vaginal discharge	**Contraindications** Hypersensitivity Personal history of deep vein thrombosis, pulmonary embolism, or anticoagulant use

TABLE 8.16 **Drug Prototype Table: Tamoxifen** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking hormonal agents:

- Assess client overall well-being prior to administration, including vital signs, weight, fatigue, bone pain, and neurovascular status.
- Review laboratory values thoroughly, including complete blood counts, electrolyte profiles, serum creatinine, liver enzymes, and bone scans.
- Be aware of the drug's black box warnings.
- Recognize and manage emergent situations such as hypersensitivity reactions.
- Assess for and provide supportive therapies as needed.
- Provide for educational, spiritual, and psychosocial needs of the client and caregivers.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a hormonal agent should:

- Report the following to the health care provider: fever, chills, productive cough, bone pain, swelling in extremities, pain in calf, chest pain, or shortness of breath.
- Remain well hydrated.
- Report side effects including sexual dysfunction, hot flashes, nausea and vomiting, mood changes, and weight gain.
- Understand the need for frequent follow-up and laboratory tests.
- Know which drug/food interactions to avoid.

The client taking a hormonal agent *should not:*

- Be around others who are ill or who have received live vaccines within 3 months.

- Garden without the use of gloves to protect hands from direct contact with the soil, which contains bacteria and mold.
- Clean feline litter boxes to avoid contact with bacteria.
- Take vaccines without consulting with their health care provider.
- Consume uncooked meats and wild game such as deer, rabbits, and pheasants.
- Begin taking new supplements or medications without consulting their health care provider.
- Become pregnant.

FDA BLACK BOX WARNING

Hormonal Agents

Tamoxifen: Serious and life-threatening events associated with tamoxifen in the risk reduction setting for clients at high risk for cancer and those with ductal carcinoma in situ include uterine malignancies, stroke, and pulmonary embolism.

Flutamide: Life-threatening liver failure has been linked to flutamide use, especially in the first 3 months of treatment.

UNFOLDING CASE STUDY

Part B

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up to Case Study Part A.

Guadalupe Himenez has returned to the clinic for her first day of chemotherapy. Her treatment course will involve a combination of agents. Today she is receiving her first dose of paclitaxel (Taxol).

3. Prior to administering the Taxol, the nurse gives Guadalupe several medications including hydrocortisone and diphenhydramine. The client questions what these medications are for. What is the best response by the nurse?
   a. "To help stimulate your white blood count."
   b. "To decrease the risk you will develop a hypersensitivity reaction to the Taxol."
   c. "To decrease the risk of respiratory problems developing."
   d. "To enhance the effectiveness of the medication."

4. In addition to the parental chemotherapy regimen, Guadalupe will take tamoxifen orally at home. The nurse instructs the client on this new medication. Which of the following statements by Guadalupe indicates the need for additional instruction?
   a. "This medication will make my menstrual periods heavier."
   b. "I will likely gain weight while taking this medication."
   c. "I might start having hot flashes."
   d. "This medication could cause nausea and vomiting."

8.4 Biologic Response Modifiers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 8.4.1 Identify characteristics of biologic response modifier drugs used to treat cancer.
- 8.4.2 Explain the indications, actions, adverse reactions, and interactions of biologic response modifier drugs used to treat cancer.
- 8.4.3 Describe the nursing implications of biologic response modifier drugs used to treat cancer.
- 8.4.4 Explain the client education related to biologic response modifier drugs used to treat cancer.

Monoclonal Antibodies and PD-1 Inhibitors

Cancer therapy has experienced an explosion of new treatments with the development of biologics. Monoclonal antibodies are a type of biologic response modifier used to treat autoimmune diseases as well as various cancer types. Rituximab is a monoclonal antibody that enables the immune system to better recognize and destroy cancer cells. These drugs pose a high risk of sensitivity reactions that include chills, fever, and anaphylaxis. Clients must be premedicated with diphenhydramine and acetaminophen to prevent or decrease risks for hypersensitivity reactions.

The newest approved class of monoclonal antibodies is PD-1 inhibitors. These drugs inhibit PD-1 proteins on T lymphocytes. When these proteins are blocked, the T lymphocytes are able to identify cancer cells and kill them more easily. Because these drugs increase the activity of T lymphocytes, a side effect of these drugs is possible development of autoimmune syndromes. Clients receiving these drugs must be carefully monitored throughout intravenous infusions for possible hypersensitivity reactions.

Growth Factor and Tyrosine Kinase Inhibitors

Growth factor inhibitors and tyrosine kinase inhibitors are also types of biologic response modifiers. Erlotinib is a tyrosine kinase inhibitor that is used to treat non-small cell lung cancer and late-stage pancreatic cancer. This drug works to prevent the growth of tumors influenced by epidermal growth factor receptors (EGFR). Cell differentiation, proliferation, and angiogenesis cannot occur when EGFR is blocked. Ibrutinib is another tyrosine kinase inhibitor used to treat leukemias and lymphomas.

Table 8.17 lists common growth factors and tyrosine kinase I inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
PD-1 Inhibitors	
Pembrolizumab (Keytruda)	200–400 mg/dose IV every 3 weeks or every 6 weeks per protocol.
Nivolumab (Opdivo)	240 mg IV every 2 weeks or 480 mg IV every 4 weeks per protocol.
Durvalumab (Imfinzi)	*Clients with a body weight ≥30 kg:* 10 mg/kg IV every 2 weeks or 1500 mg every 4 weeks. *Clients with a body weight <30 kg:* 10 mg/kg IV every 2 weeks.
Atezolizumab (Tecentriq)	840 mg IV every 2 weeks or 1200 mg every 3 weeks or 1680 mg every 4 weeks.
Biologic Response Modifiers	
Rituximab (Rituxan)	375–500 mg/m^2 IV; frequency varies by cancer type (premedicate per protocol).
Tyrosine Factor/Growth Factor Inhibitors	
Erlotinib (Tarceva)	100–150 mg/day orally on empty stomach.
Ibrutinib (Imbruvica)	420 mg/day orally.

TABLE 8.17 **Drug Emphasis Table: Biologics and Biologic Response Modifiers** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

One of the most critical adverse reactions of biologic therapy is hypersensitivity reactions. These may occur suddenly, especially during the initial treatment, and may be severe and life-threatening. Any premedication must be given, and emergency drugs such as epinephrine should be available. Biologic therapies are also associated with skin reactions that may be severe. Erlotinib has been shown to cause renal dysfunction, arrhythmias, hepatotoxicity, and gastrointestinal perforation. Clients may also develop widespread, severe acneiform rashes. In addition to severe hypersensitivity reactions, rituximab is also associated with cardiotoxicity, nephrotoxicity, leukoencephalopathy, bowel obstruction or perforation, tumor lysis syndrome, neutropenia, and infection.

Table 8.18 is a drug prototype table for biologic response modifiers featuring pembrolizumab. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Biologic response modifier, PD-1 inhibitor **Mechanism of Action** Inhibits PD-1 to increase T lymphocyte activity	**Drug Dosage** 200–400 mg/dose IV every 3 weeks or every 6 weeks per protocol.
Indications Melanoma Non-small cell lung cancer Head and neck cancer Classical Hodgkin lymphoma Primary mediastinal large B-cell lymphoma (PMBCL) Urothelial cancer Gastric cancer Cervical cancer Hepatocellular carcinoma Merkel cell carcinoma Renal cell cancer Cutaneous squamous cell carcinoma Small cell lung cancer Esophageal cancer Endometrial cancer Triple-negative breast cancer **Therapeutic Effects** Reduction/elimination in cancerous cell expressions of PD-1	**Drug Interactions** Thalidomide **Food Interactions** None reported
Adverse Effects Infusion-related reactions Severe, possibly fatal immune-mediated reactions	**Contraindications** No significant contraindications Caution: Severe, possibly fatal immune-mediated reactions may occur May have severe infusion-related reactions Embryo-fetal toxicity

TABLE 8.18 **Drug Prototype Table: Pembrolizumab** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking biologic and biologic response modifying agents:

- Assess client overall well-being prior to chemotherapy administration including vital signs, hydration status, oral mucosa, skin, weight, cardiac function, bowel pain, level of consciousness changes, and signs of neuropathy.
- Review laboratory values thoroughly, including complete blood counts, electrolyte profiles, serum creatinine, and liver enzymes.
- Observe clients for adverse effects before, during, and after treatment.
- Ensure patency of intravenous access sites and monitor these frequently during drug administration.
- Adhere to proper handling and administration procedures when administering biologic therapies.
- Be aware of the drug's black box warnings.
- Recognize and manage emergent situations such as hypersensitivity reactions.
- Assess for and provide supportive therapies as needed.

- Provide for educational, spiritual, and psychosocial needs of the client and caregivers.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a biologic or biologic response modifying agent should:

- Know signs and symptoms to report to the health care provider: fever, chills, productive cough, urinary symptoms, skin reactions, chest pain, confusion, and level of consciousness changes.
- Report side effects including nausea and vomiting and skin reactions.
- Know how to care for long-term intravenous accesses at home.
- Understand the need for frequent follow-up and laboratory tests.
- Know which drug/food interactions to avoid.
- Understand the need for regular follow-up for early identification of long-term effects and secondary malignancies.

The client taking a biologic or biologic response modifying agent *should not:*

- Be around large crowds or around others who are sick to decrease the risk of infection.
- Become dehydrated.

FDA BLACK BOX WARNING

Rituximab

Rituximab may cause fatal infusion-related reactions, most often with the initial treatment. Mucocutaneous reactions, reactivation of hepatitis B, and progressive multifocal leukoencephalopathy have also been associated with rituximab.

Chapter Summary

This chapter discussed the causes and development of cancer based on different theories of mutational changes. These changes included the influences of stress, genetics, and environmental exposures as causes of cancer formation. The chapter also covered how chemotherapy works and the effects that chemotherapy has on both normal and abnormal cells. A summary of different major classes of chemotherapy and individual agents was included. Considerations for both safely providing chemotherapy and monitoring clients for adverse effects were discussed. Supportive therapies necessary when administering chemotherapeutic agents were also included.

Key Terms

adenocarcinoma cancer development arising from the glandular tissues that line body organs
alopecia abnormal loss of body hair
benign not causing harmful effects
chemotherapy drug therapy focused on killing cancer cells
embolization the introduction of a foreign object (bone fragments, cells, air, blood clot) into the bloodstream
erythrocytes a red blood cell
erythrocytopenia a decrease below normal levels of circulating erythrocytes
extravasate the leakage of a vesicant drug into the tissues surrounding the intravenous infusion site
febrile neutropenia occurrence of a fever during a period of neutropenia, when the risk of infection is higher than normal
fibrosis the thickening or scarring of connective tissue
granulocytes a white blood cell type; assists in fighting invading organisms
granulocytopenia a decrease below normal levels of circulating granulocytes
hematological cancers cancer development arising from bone marrow cells
hemorrhagic cystitis inflammation of the bladder lining, resulting in bleeding and hematuria
leukemia cancer development arising from leukocytes
leukocytes a white blood cell type; assists in fighting invading organisms
leukopenia a decrease below normal levels of circulating leukocytes
mesna a medicine used to prevent hemorrhagic cystitis in clients receiving chemotherapy
metastasize spread to other sites in the body
mucositis inflammation and ulceration of oral and/or gastrointestinal mucous membranes; often a side effect of chemotherapy or radiation therapy
multiple myeloma cancer development arising from plasma cells
mutation a change in the nucleic acid sequence in a cell
myelosuppression decreased production of blood cells by the stem cells in the bone marrow
nadir the point after a chemotherapy treatment at which a client's blood cell counts are at the lowest level before recovery
neoangiogenesis the ability of a tumor mass to grow new vascularity
neutropenia a decrease below normal levels of circulating neutrophils
neutrophils a white blood cell type; assists in fighting invading organisms
non-Hodgkin lymphoma cancer development arising from lymph cells
oncogene a mutated gene that has the potential to cause cancer development
pancytopenia a decrease below normal levels of all circulation blood cell lines including white blood cells, red blood cells, and platelets
plant alkaloid naturally occurring organic nitrogen-containing bases derived from plants
pulmonary toxicity lung damage
secondary cancer a cancer that develops after exposure to treatment for a previous cancer
squamous cell carcinoma cancer development arising from skin cells
thrombocytes a platelet: a cell that helps to form blood clots
thrombocytopenia a decrease below normal levels of circulating thrombocytes
tumor lysis syndrome a condition occurring after administration of chemotherapy resulting in cell death that releases cellular contents into the blood
vesicant any intravenous drug capable of causing blistering and tissue damage should extravasation occur

Review Questions

1. The nurse is providing instruction to a client who will be receiving chemotherapy that selectively kills cancer cells without harming normal cells. Which type of chemotherapy is the nurse describing to the client?

a. Adjuvant therapy
b. Neoadjuvant therapy
c. Targeted therapy
d. Biologic therapy

2. The nurse is reviewing the medical record for a client receiving doxorubicin for breast cancer. The record shows that the client has received a lifetime total of 360 mg/m^2. Which action should the nurse take?
a. Continue with treatment and routine monitoring because this is within safe lifetime dose limits
b. Call the pharmacy to ask that the cumulative dose be reduced
c. Notify the provider that the client needs a dose reduction
d. Notify the client that the next chemotherapy appointment will be delayed

3. The nurse is checking the medication orders for a client receiving fluorouracil for the treatment of colon cancer. Which medication should the nurse anticipate will be ordered with fluorouracil?
a. Leucovorin
b. Phenytoin
c. Acetaminophen
d. Diphenhydramine

4. Which statement made by a client indicates to the nurse that the client understands self-care during myelosuppressive chemotherapy?
a. "I will include more salads in my diet."
b. "I am excited about visiting my granddaughter's preschool class."
c. "I am going to increase my protein intake by eating venison my family prepared."
d. "My sister will be caring for my cat while I am undergoing treatment."

5. The nurse is caring for a client receiving pembrolizumab. What should the nurse should monitor the client for signs of?
a. Vitamin D deficiency
b. Pernicious anemia
c. Immune-mediated destruction
d. Severe neutropenia

6. Which finding should the nurse expect in a client with acute myelogenous leukemia who has developed tumor lysis syndrome?
a. Hypokalemia
b. Hypophosphatemia
c. Hypocalcemia
d. Alkalosis

7. Which information would the nurse give to a 67-year-old female client receiving tamoxifen to treat breast cancer?
a. Tamoxifen can cause muscle or joint pain.
b. This medication is administered intramuscularly.
c. Liver function tests need to be closely monitored.
d. Tamoxifen is taken for 5 years.

8. A client diagnosed with breast cancer is scheduled to begin initial treatment with doxorubicin. Prior to administering the first dose of doxorubicin, the nurse notes that the client's left ventricular ejection fraction is 58%. Which action should the nurse take?
a. Hold the medication and call the prescriber
b. Administer the medication as prescribed
c. Notify the prescriber and request a reduced dose

d. Administer the medication, but at a reduced rate

9. The nurse is reviewing laboratory reports for a client receiving chemotherapy and notes an absolute neutrophil count of 1.4 cells/mcL. Which order should the nurse anticipate?
   a. Epoetin alfa
   b. Filgrastim
   c. Packed red blood cells
   d. Interferon A

10. Which premedication order will the nurse anticipate being ordered to administer prior to administering rituximab?
   a. Diphenhydramine and acetaminophen
   b. Phenytoin and acetaminophen
   c. Corticosteroid
   d. Aspirin and ondansetron

CHAPTER 9
Introduction to the Nervous System

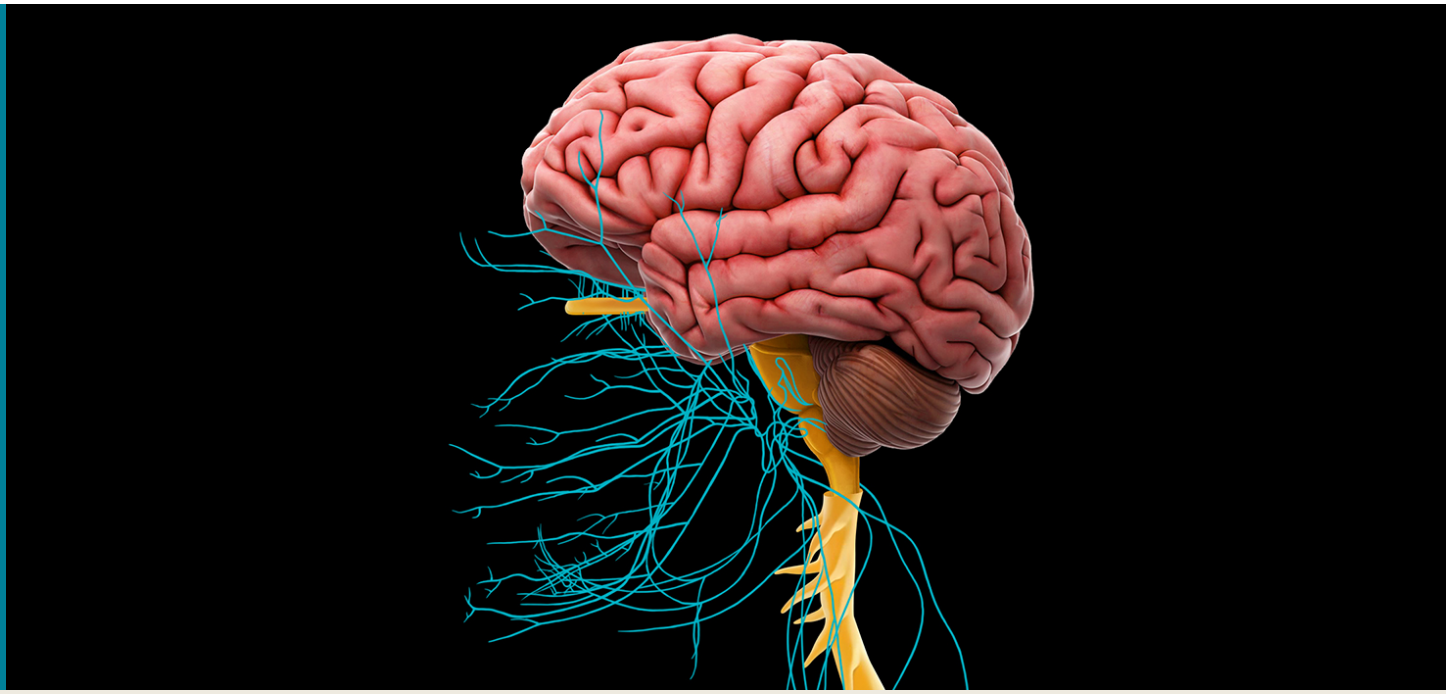


FIGURE 9.1 The nervous system, the body's control center, consists of the brain, the spinal cord, and a very complex system of nerves. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Neurological disorders affect the body's autonomic, peripheral, and central nervous system. These disorders may occur at different points in the lifespan of an individual and for a variety of reasons. The severity of neurological disorders also varies greatly, with some disorders being mild and self-limiting to other disorders that may be quite debilitating or even life-threatening. Some examples of neurological disorders are migraines, non-migraine headaches, multiple sclerosis, dementia such as Alzheimer's disease, Parkinson's disease, brain tumors, spinal cord injuries, stroke, and epilepsy. Clients with a neurological disorder may experience a wide range of signs and symptoms. Therefore, a thorough neurological assessment is vital to detect deficits or changes in baseline neurological functioning. Signs and symptoms of a neurological disorder include headaches, memory or sensation loss, muscle weakness, tremors, nausea/vomiting, loss of bowel and/or bladder control, seizures, impacted speech, aphasia (trouble speaking), dysphagia (swallowing difficulties), intractable pain, blindness, and paralysis, all of which may vary in severity from mild to complete loss (Sargsyan, 2020; Shahrokhi & Asuncion, 2023). The occurrence of neurological disorders may be related to factors including genetics, infections, trauma, autoimmune reactions, or degenerative processes.

The Pan American Health Organization (PAHO) identified the overall incidence of noncommunicable neurological disorders across the Americas. Neurological disorders related to death and disability were recognized as a global public health challenge and are expected to continue increasing as the population ages. The United States is the highest ranked country from the region of the Americas for age-standardized death rates related to noncommunicable neurological disorders. Females were more affected (60%) than males (40%), but males had a slightly higher death rate compared to females (33.1 per 100,000 and 32.2 per 100,000, respectively) (PAHO,

2021). Nationally, treatment of neurological disorders is also recognized as a public health objective. The Healthy People 2030 objectives focus on various health conditions related to neurological disorders (i.e., dementia, stroke, sensory or communication disorders, and mental health disorders) (Office of Disease Prevention and Health Promotion, 2021).

TRENDING TODAY

Tracking the Epidemiology of Neurological Conditions

The National Neurological Conditions Surveillance System (https://openstax.org/r/cdcsurveillance) (NNCSS) (CDC, 2023) is a national surveillance system overseen by the Centers for Disease Control and Prevention (CDC) that tracks the epidemiology of neurological disorders. The aim of the NNCSS is to use the gathered epidemiological data to extend knowledge about neurological disorders and future research efforts to investigate related causes, diagnoses, and treatment.

9.1 Introduction to the Nervous System

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 9.1.1 Define the nervous system.
- 9.1.2 Identify the purpose of the nervous system and how it affects the body.

The Nervous System

The **nervous system** is composed of the central nervous system (CNS) (i.e., the brain and the spinal cord) and the peripheral nervous system (PNS) (i.e., the nerves that extend from the spinal cord to the body). The PNS is subdivided into the somatic nervous system and the autonomic nervous system. Together the CNS and PNS communicate with each other, the organs, and the body to promote **homeostasis** (see Figure 9.2).

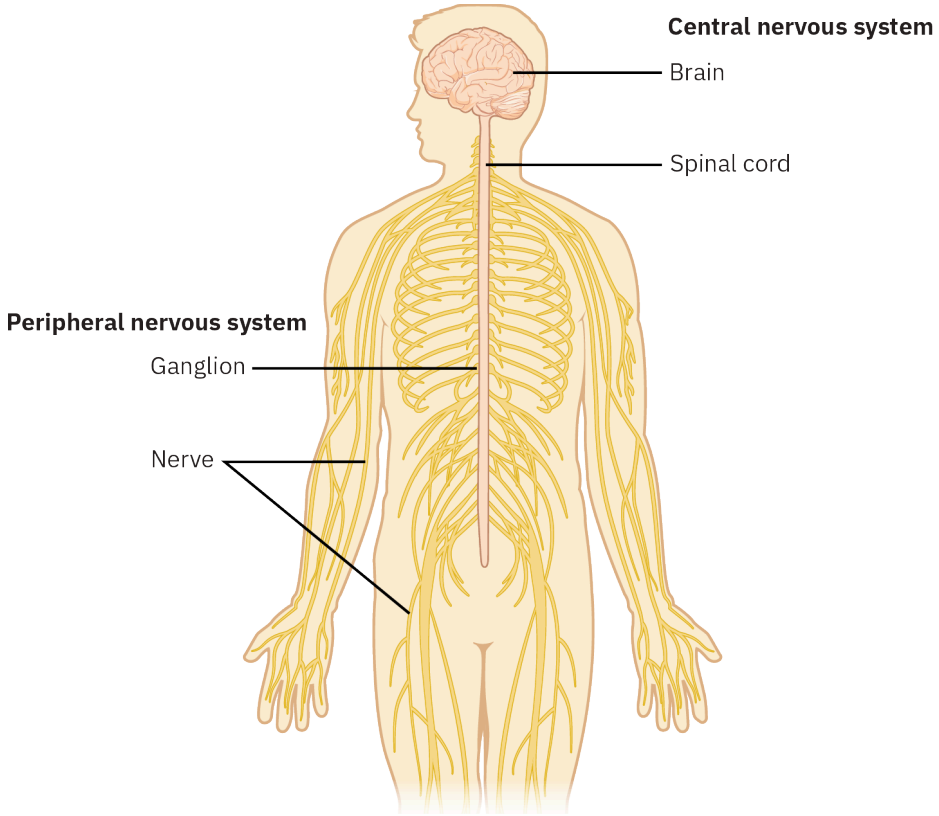


FIGURE 9.2 The CNS contains the brain and spinal cord; the PNS is composed of the nerves that branch out from the brain and spinal cord and serve as the communication between the CNS and the body. (credit: modification of work from Anatomy and Physiology 2e. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The Nervous System and the Human Body

The nervous system serves as the communication and control system for the human body. This control system, which is essentially composed of all of the nerve cells in the body, regulates everything that we remember, think, and say. It also controls movement and sensation as well as the autonomic responses of breathing, blood pressure, and digestion. It has the unique ability to interact with the environment as well as regulate the activities of the body's internal organs. Essentially, the nervous system propels the other systems of the body; no other system can function without input from the nervous system. It does so by its composition of structures that transmit electrical and chemical signals between the organs, tissues, and brain.

9.2 Structure and Function of the Nervous System

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 9.2.1 Discuss the structure and function of the nervous system and neurons.
- 9.2.2 Recognize terminology related to the nervous system.

Overview of the Nervous System and Neurons

Within the PNS, the autonomic nervous system (ANS) controls involuntary processes and regulates vital functions such as heart rate, digestion, respiration, and glandular secretion, while the somatic nervous system (SNS) consists of motor and sensory pathways that are associated with the voluntary movement of skeletal muscles. The PNS relays information between the CNS and the rest of the body via **neurons**, the basic units of the nervous system. The brain contains approximately 100 billion neurons (Chen, 2023). Glial cells are also found in nervous tissue and serve to support neurons. While glial cells are unable to generate action potentials, they play a key role in the development, support, and protection of neurons.

Structurally, neurons consist of three main components: the cell body (soma), dendrites, and an axon. The cell body contains the nucleus and other essential cellular components. Dendrites branch out from the cell body, acting as receivers of signals from other neurons. The axon is a long, slender extension that carries electrical impulses away from the cell body toward other neurons or target cells. See Figure 9.3 for a visual representation of a neuron.

Neurons grouped together are bundles of nerve cells that transmit electrochemical information via a process known as **neurotransmission**. **Neurotransmitters**, which are chemical messengers, are stored in the axon terminals of presynaptic neurons. These neurotransmitters then bind to receptors on the receiving neuron's dendrites, transmitting the signal across the synapse and allowing the information to be passed on. The two main types of synapses are electrical and chemical. Electrical synapses have direct communication by physical connections. With chemical synapses, when an electrical signal reaches the end of an axon, it triggers the release of one of the chemical messengers (or neurotransmitters) into the chemical synapse, which is the small gap between neurons. If the postsynaptic cell is also a neuron, there may be a subsequent increase or decrease in firing rate. However, if the postsynaptic cell is a muscle cell, muscle contraction or relaxation can result. If the postsynaptic cell is a glandular cell, there will be an increase or decrease in secretion.

The connections formed by neurons create neural networks, which serve as the framework for the brain's ability to process and integrate information. These networks allow for the transmission of sensory input, coordination of motor functions, and the execution of higher cognitive processes such as learning, memory, and decision-making.

Neurons are diverse in terms of their structure, function, and location within the nervous system. Sensory neurons transmit information from sensory organs to the brain, motor neurons carry signals from the brain to muscles and glands, and interneurons facilitate communication between different neurons within the central nervous system.

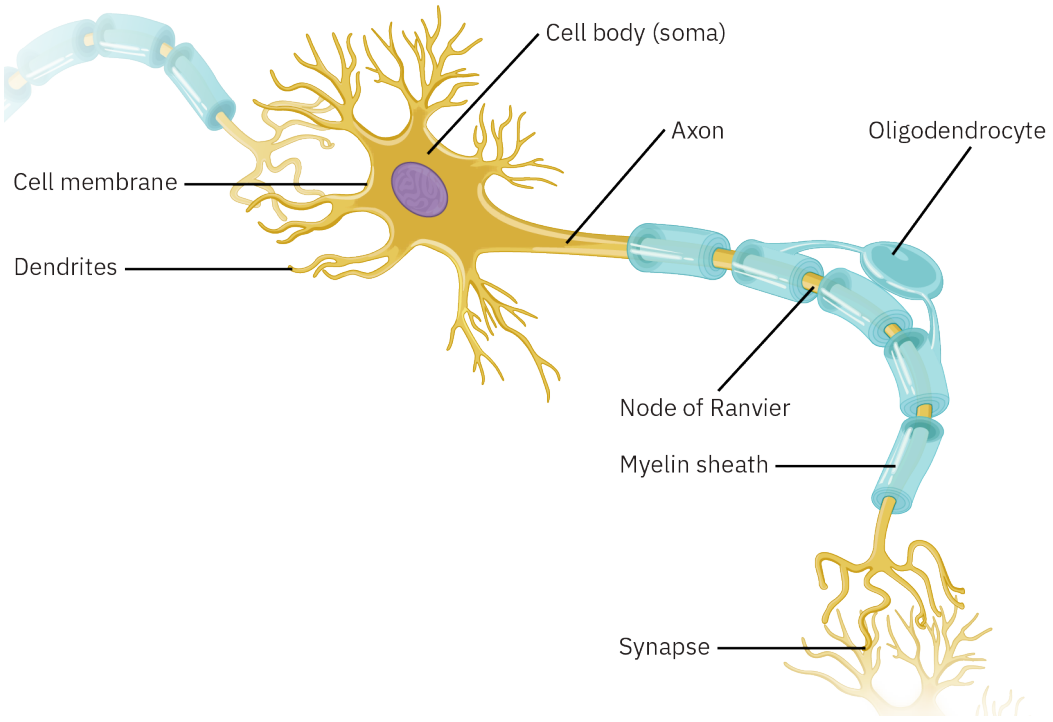


FIGURE 9.3 The major parts of the neuron are labeled on a multipolar neuron from the CNS. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Overview of the Brain

The brain has four main components: the cerebrum, cerebellum, brain stem, and limbic system (see Figure 9.4).

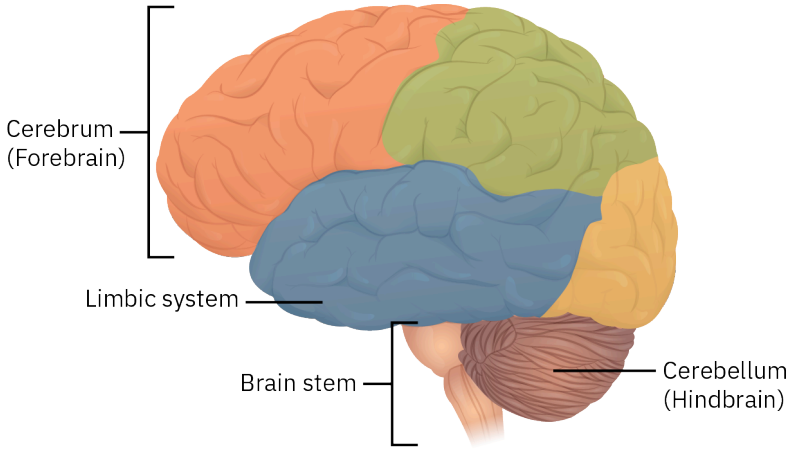


FIGURE 9.4 Basic brain structures include the cerebrum, cerebellum, brain stem, and the limbic system. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The cerebrum is divided into two hemispheres that are connected by the corpus callosum. The lobes and structures within the left and right hemispheres are contained in both hemispheres with the exception of the pineal body. The pineal body is an endocrine gland located between the two cerebral hemispheres. Each hemisphere is divided into four lobes: the frontal lobe, parietal lobe, temporal lobe, and the occipital lobe.

The cerebellum, located below the cerebrum, controls coordination of movement and postural adjustment.

The brain stem is composed of the midbrain, pons, and medulla oblongata. The brain stem is responsible for basic involuntary respiratory and cardiovascular functions.

The limbic system is composed of a thalamus, hypothalamus, hippocampus, and amygdala. These structures regulate various bodily functions (e.g., activity, sensation, emotion, temperature, appetite, endocrine function, and sexual drive).

The spinal cord is approximately 18 inches long, encased in the spinal column, and surrounded by cerebrospinal fluid. The spinal cord originates from the brain stem and extends down the back. The spinal cord is protected by bone segments, or vertebrae, supported by discs and ligaments. The vertebrae are identified by their relative position on the body. The spinal cord is divided into four sections (see Figure 9.5):

- Cervical vertebrae (C1–C7) in the neck
- Thoracic vertebrae (T1–T12) in the upper back and attached to the ribcage
- Lumbar vertebrae (L1–L5) in the lower back
- Sacral vertebrae (S1–S5) in the pelvis

Nerves extend from the spinal cord and spread throughout the body. There are 31 pairs of spinal nerves. Spinal nerves are the conduit for communication between the CNS and the PNS.

Peripheral Nervous System

The peripheral nervous system (PNS) delivers signals between the central nervous system (CNS) and the body. The PNS contains both motor neurons and sensory neurons. Motor neurons coordinate signals that correspond to muscle and gland activity, while sensory neurons provide the signals to sensory organs. The somatic nervous system and autonomic nervous system are both types of motor neurons. The somatic nervous system regulates voluntary movements of skeletal muscles. The autonomic nervous system regulates involuntary responses by controlling the cardiac muscle and smooth muscle contractions in addition to gland activity.

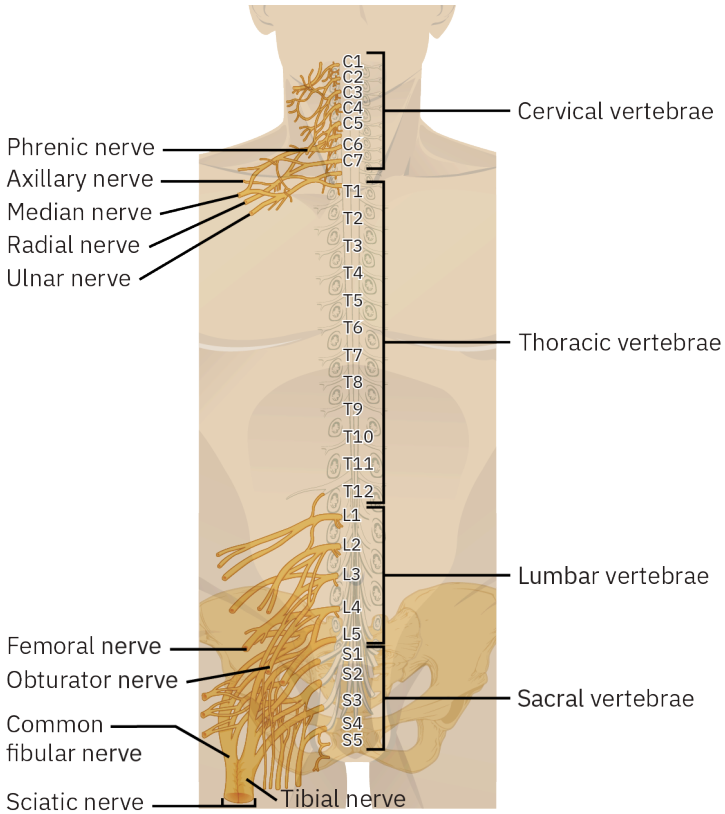


FIGURE 9.5 The spinal cord is divided into four sections, and there are 31 pairs of spinal nerves. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The autonomic nervous system is divided into the sympathetic and parasympathetic nervous systems. The sympathetic nervous system is commonly known as the “fight or flight” system and is activated when the body is under actual or perceived stress to ready the body’s response to a potential threat. Activation results in the following physiological changes:

- Increased heart rate, heart contraction, and blood pressure
- Shunting of blood to skeletal muscle
- Bronchial dilation

- Pupillary dilation
- Decreased salivation and digestion
- Glucose release
- Epinephrine and norepinephrine secretion, resulting in peripheral vasoconstriction
- Bladder relaxation

Conversely, the parasympathetic system is known as the "rest and digest" system. Activation of the parasympathetic nervous system translates into a series of bodily reactions that are, generally but not always, opposite of the reactions seen in the sympathetic nervous system. These changes are:

- Slowed heart rate, heart contraction, and decreased blood pressure
- Bronchial constriction
- Pupillary constriction
- Increased salivation and digestion
- Bladder constriction

9.3 Characteristics of Drugs to Treat Nervous System Disorders

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 9.3.1 Describe the main neurotransmitters and their functions.
- 9.3.2 Define characteristics of drugs to treat nervous system disorders.

Neurotransmitters

Neurotransmitters play a crucial role in the communication between neurons in the nervous system. Neurotransmitters are chemical messengers that transmit signals across the chemical **synapses**, enabling various functions and processes in the body, including signaling to release neurotransmitter molecules. Synapses are composed of three components: the presynaptic terminal, the post-synaptic terminal, and the synaptic cleft. Synaptic vesicles, containing neurotransmitter molecules, are located on the presynaptic terminal at the end neuron's axon. Subsequently, the postsynaptic terminal uses specialized protein receptors to bind to these neurotransmitters. Neurotransmitters result in an action, inaction, or inhibition of a neuron (see Figure 9.6). When neurotransmitter levels are imbalanced or disrupted, it can lead to pathological conditions and disorders.

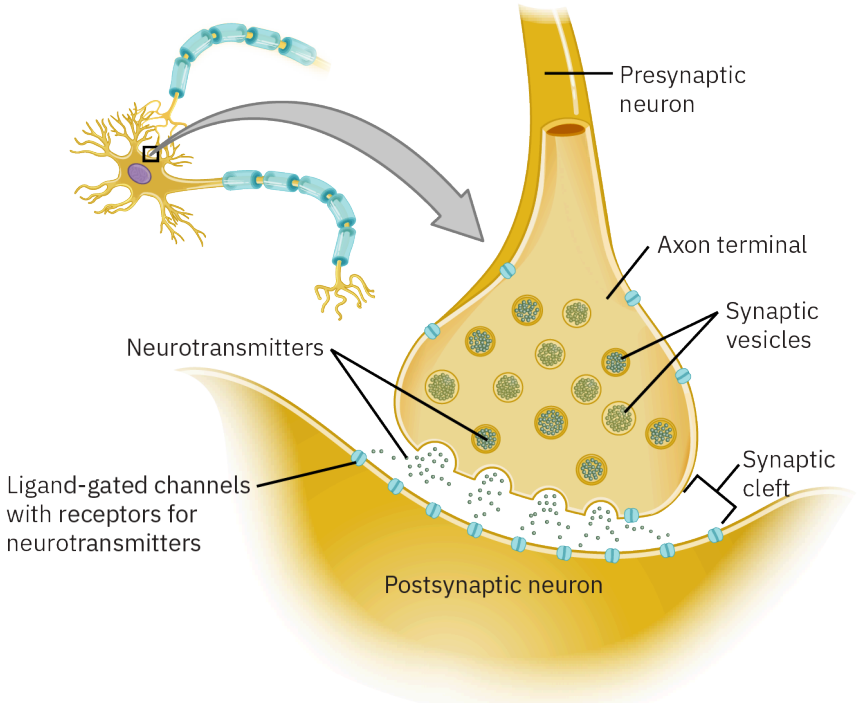


FIGURE 9.6 The synapse is the space between the axon of one neuron and the dendrite of another. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

It is important to note that neurotransmitter imbalances are just one aspect of the complex mechanisms underpinning pathological conditions. Many disorders involve a combination of genetic, environmental, and neurochemical factors. Diagnosis and treatment of these conditions often require a comprehensive approach involving various therapies and medications targeting specific neurotransmitter systems.

The main neurotransmitters of the nervous system, function, and potential pathology are shown in Table 9.1. (The items in the "Potential Pathology" column are provided as examples, not as an exhaustive list.)

Neurotransmitter	Function	Potential Pathology
Acetylcholine	• Sleep • Arousal • Pain • Muscle contractions • Movement • Memory	Low levels of acetylcholine have been noted in Alzheimer's disease and myasthenia gravis.
Norepinephrine	• Mood • Cognition • Perception • Locomotion • Cardiovascular function • Sleep • Arousal	Imbalances in norepinephrine levels have been associated with various disorders, including attention deficit hyperactivity disorder (ADHD) and mood disorders.
Dopamine	• Movement • Coordination • Emotions • Voluntary judgment • Prolactin release • Reward • Pleasure	Imbalanced levels of dopamine have been associated with psychiatric and neurological disorders, including schizophrenia, depression, and Parkinson's disease.
Serotonin	• Sleep • Arousal/libido • Appetite • Mood • Aggression • Pain • Coordination • Judgment	Serotonin pathology is typically associated with depression but is also associated with bowel motility, bladder control, and cardiovascular function.
Histamine	• Wakefulness • Pain • Inflammatory response	Histamine plays a role in asthma, bronchospasm, and mucosal edema as well as multiple sclerosis.

TABLE 9.1 **Neurotransmitters and Pathology** (sources: adapted from Sam & Bordoni, 2023; Sheffler et al., 2023)

Neurotransmitter	Function	Potential Pathology
Gamma-aminobutyric acid (GABA)	• Decreased neuron activity • Decreased body activity	GABA, considered primarily an inhibitory neurotransmitter, has been implicated in anxiety disorders, epilepsy, and sleep disorders.
Glutamate	• Sensory information relay • Various motor and spinal reflexes regulation • Memory and learning	Glutamate is the primary excitatory neurotransmitter; its dysfunction has been related to Alzheimer's disease and Parkinson's disease.

TABLE 9.1 **Neurotransmitters and Pathology** (sources: adapted from Sam & Bordoni, 2023; Sheffler et al., 2023)

Nervous System Drug Properties

The primary neurotransmitters of the PNS are acetylcholine, norepinephrine, and epinephrine.

Nerves that release acetylcholine are called cholinergic nerves. Nicotinic receptors and muscarinic receptors are the two subtypes of cholinergic receptors. Cholinergic receptor activation results in tachycardia, hypertension, increased tone, and motility of the digestive tract. Drugs that increase or stimulate the release of acetylcholine are known as **parasympathomimetic** due to their mimicking of the parasympathetic nervous system. Drugs that block acetylcholine are known as anticholinergic, cholinergic-blocking, or parasympatholytic and result in inhibition of the parasympathetic nervous system and sympathetic nervous system induction.

Adrenergic receptors mediate the response to epinephrine (adrenaline) and norepinephrine. The subtypes of adrenergic receptors are the alpha receptors (alpha1 and alpha2) and beta receptors (beta1, beta2, and beta3). Adrenergic drugs, also referred to as **sympathomimetics**, mimic the sympathetic nervous system response. Adrenergic antagonists block adrenergic receptors and reduce the effects of norepinephrine. Some drugs may target the activation of one receptor or activate multiple receptors. See Table 9.2 for an overview of autonomic receptors and subsequent responses.

Primary Neurotransmitter	Receptor	Response
Norepinephrine	Alpha1	Mydriasis (pupil dilation), smooth muscle contraction
	Alpha2	Inhibited norepinephrine release
	Beta1	Increased heart rate, increased heart contraction force, renin release
	Beta2	Smooth muscle inhibition
	Beta3	Increased lipolysis
Acetylcholine	Nicotinic	Stimulates smooth muscle and gland secretions
	Muscarinic	Decreased heart rate and heart contraction force

TABLE 9.2 **Autonomic Receptors and Anticipated Actions** (sources: adapted from information in Alhayek & Preuss, 2023; Carlson & Kraus, 2023; Farzam et al. 2023; Waxenbaum et al., 2023)

Autonomic Nervous System Stimulant and Blocker Characteristics

Any pathological process that causes a disruption in the homeostasis between the SNS and the PNS may cause one of these branches to become overexcited while causing the other system to be extremely inhibited (Clar & Sharma, 2023). A wide range of symptoms may occur due to this disruption in homeostasis, and medications may be used to restore homeostasis. There are four groups of medications that are used to restore homeostasis between the SNS and PNS, and they are classified on how they affect the ANS (Clar & Sharma, 2023):

1. Cholinomimetics/cholinesterase antagonists include medications that are used in the treatment of urinary retention, glaucoma, smoking cessation, the diagnosis and treatment of myasthenia gravis, and the treatment of Alzheimer's disease.
2. Anticholinergics can be used in the treatment of bradycardias, bronchospasm, postoperative nausea and vomiting, bladder spasms, and diarrhea.
3. Adrenoreceptor agonists/sympathomimetics include medications that are indicated for the treatment of hypertension, asthma (bronchodilators), and Parkinson's disease. The drugs dobutamine, phenylephrine, and epinephrine are also in this category; they are used to treat hypotension, heart failure, cardiogenic shock, and anaphylaxis.
4. Adrenoreceptor antagonists are indicated in the treatment of urinary retention (in benign prostatic hyperplasia), hypertension, dysrhythmias, angina, heart failure, and migraine prophylaxis.

It is important to remember that the four categories just discussed act as either an agonist or an antagonist for the receptors mentioned in Table 9.2.

Sympathetic Nervous System Stimulant and Blocker Characteristics

Medications that are classified as stimulants cover a wide range of drugs that increase the activity of the central nervous system (Farzam et al., 2023). Some of the medications in this category treat attention deficit hyperactivity disorder, narcolepsy, asthma, obesity, sinus congestions, and hypotension. Drugs in this category range from caffeine to amphetamines and from legal to illegal.

Since the sympathetic nervous system plays a rather large role in the regulation of the circulatory system and in the regulation of blood pressure, many medications that act to block the sympathetic nervous system reduce blood pressure (see Antihypertensive and Antianginal Drugs). Some of these drugs work by affecting the central nervous system, and others work at peripheral neuromuscular sites.

Parasympathetic Nervous System Stimulant and Blocker Characteristics

As mentioned earlier in this section, parasympathomimetic drugs mimic the physiologic effects of the parasympathetic nervous system by acting as the muscarinic acetylcholine receptors. Bethanechol, which treats urinary retention; carbachol, which is used in the treatment of open-angle glaucoma; and pilocarpine, which treats both open- and closed-angle glaucoma, are examples of direct-acting parasympathomimetic drugs. There are other indirect-acting parasympathomimetic drugs that cause an increase in the synaptic concentration of acetylcholine, which result in the extended stimulation of cholinergic receptors throughout both the CNS and PNS (Patel & Dewaswala, 2023).

Chapter Summary

This chapter provided an overview of the nervous system. The nervous system is divided into two main parts: the central nervous system and the peripheral nervous system. The central nervous system consists of the brain and spinal cord. The peripheral nervous system consists of the autonomic nervous system and the somatic nervous system. The autonomic nervous system is further divided into the sympathetic nervous system (i.e., the fight or flight system) and the parasympathetic nervous system (i.e., the rest and digest system).

Neurons are the fundamental units of the nervous system. Neurons send electrical signals to other neurons via chemical messengers, known as neurotransmitters. The primary neurotransmitters of the nervous system are acetylcholine, norepinephrine, dopamine, serotonin, histamine, gamma-amino-butyric acid (GABA), and glutamate. Acetylcholine, epinephrine, and norepinephrine are the fundamental neurotransmitters within the autonomic nervous system. Drugs that stimulate acetylcholine (cholinergic medications) are known as parasympathomimetic. Drugs that block acetylcholine (anticholinergic) result in sympathetic stimulation. Drugs that stimulate the sympathetic nervous system are adrenergic receptor agonists or sympathomimetic.

Key Terms

homeostasis maintenance of equilibrium and stability necessary for human life

nervous system system that includes the brain and spinal cord (the central nervous system) and an intricate network of nerves (the peripheral nervous system)

neurons the basic units of the nervous system

neurotransmission the transmission of electrochemical information between neurons

neurotransmitter a chemical messenger that results in action, inaction, or inhibition of a neuron

parasympathomimetic drugs that stimulate or mimic the parasympathetic nervous system (rest and digest)

sympathomimetics drugs that stimulate or mimic the sympathetic nervous system (fight or flight)

synapse the space between two neurons

Review Questions

1. The nurse is caring for a client who has sustained an ischemic stroke. The nurse recognizes that the client is experiencing deficits in which part of the nervous system?
    a. Peripheral nervous system
    b. Central nervous system
    c. Somatic nervous system
    d. Autonomic nervous system

2. Parkinson's disease is associated with balance alterations. Which area is responsible for coordination of movement?
    a. Cerebrum
    b. Medulla
    c. Pons
    d. Cerebellum

3. The nurse is caring for a client wearing a neck brace. The client reports the provider informed them that their "neck fracture" may cause some nerve disturbances. Which region of the spinal cord is involved?
    a. Cervical vertebrae
    b. Thoracic vertebrae
    c. Sacral vertebrae
    d. Lumbar vertebrae

4. Which specific part of the nervous system involves regulation of involuntary responses of cardiac muscle, smooth muscle contraction, and gland activity?
    a. Peripheral nervous system
    b. Central nervous system

c. Somatic nervous system
d. Autonomic nervous system

5. The nurse is gathering an admission history from a newly admitted client. The nurse observes that the client appears calm and they have relaxed breathing. Which specific part of the nervous system is activated?
a. Peripheral nervous system
b. Sympathetic nervous system
c. Parasympathetic nervous system
d. Autonomic nervous system

6. The client reports feelings of anxiety related to perceived threats. Which specific part of the nervous system is activated related to this client's reports?
a. Peripheral nervous system
b. Sympathetic nervous system
c. Parasympathetic nervous system
d. Autonomic nervous system

7. Which communication process is involved in the sending and receiving of electrical signals within the nervous system?
a. Neuron
b. Neurotransmission
c. Homeostasis
d. Neurological regulation

8. What is the most common neurotransmitter of the autonomic nervous system?
a. Acetylcholine
b. Serotonin
c. Histamine
d. Glutamate

9. The client is prescribed a medication that stimulates acetylcholine. Which specific part of the nervous system would be affected?
a. Somatic
b. Parasympathetic
c. Sympathetic
d. Central nervous system

10. The client reports being prescribed a medication that will decrease their heart rate and the heart contraction force. Which receptor would be indicated in this medication?
a. Nicotinic
b. Alpha1
c. Beta3
d. Beta1

CHAPTER 10

Drugs to Treat Myasthenia Gravis and Alzheimer's Disease

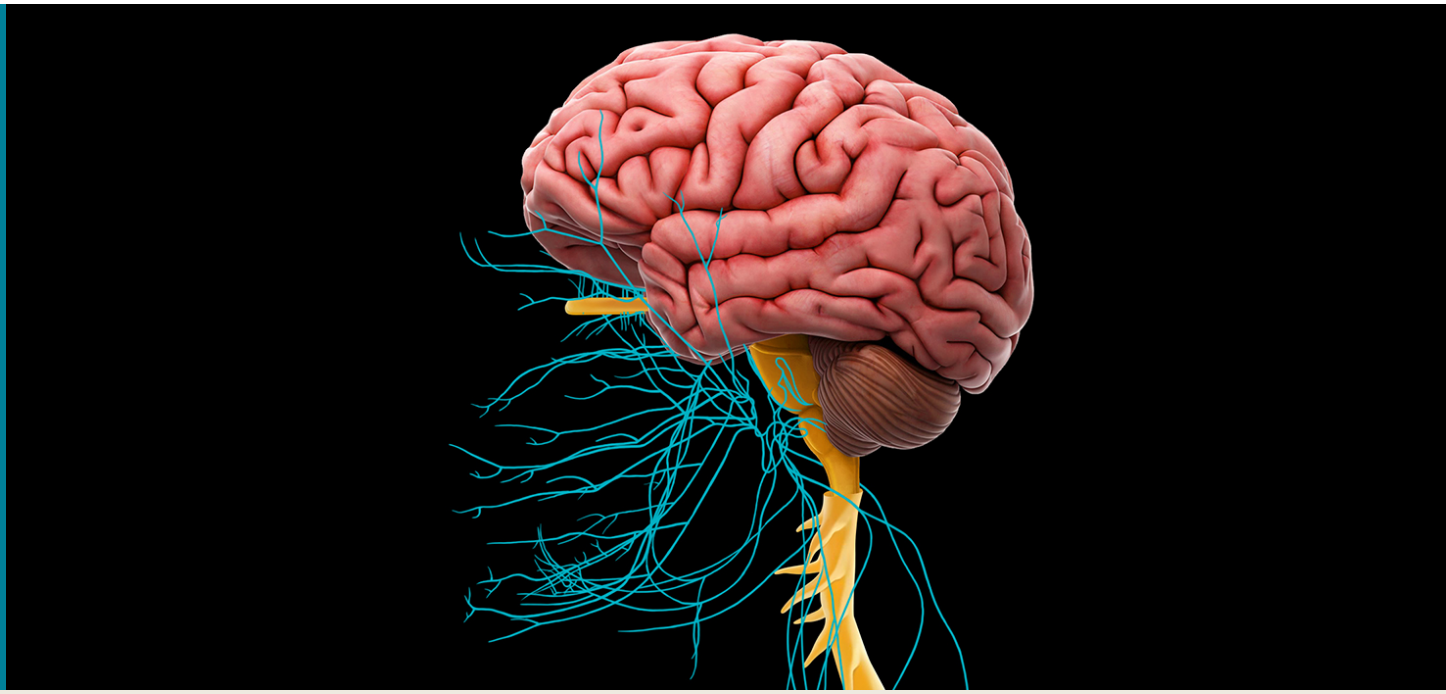


FIGURE 10.1 The nervous system, the body's control center, consists of the brain, the spinal cord, and a complex system of nerves. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The peripheral nervous system (PNS) is divided into two main subdivisions: the somatic motor system and the autonomic nervous system (ANS). The somatic nervous system controls voluntary muscle movement, and the autonomic nervous system is responsible for regulating numerous involuntary functions, such as the heart, secretory glands, and smooth muscle. The ANS is further divided into the **parasympathetic nervous system** (PSNS) and **sympathetic nervous system** (SNS) (see Figure 10.2). The PSNS relaxes the body and maintains certain life-sustaining properties such as digestion and excretion. The SNS is involved in the fight-or-flight response by preparing the body to deal with stressors. There are two primary types of receptors within the PNS: **cholinergic receptors** and **adrenergic receptors**. Cholinergic receptors are activated by the neurotransmitter **acetylcholine** (**ACh**) and can be activated by endogenous or exogenous substances. Adrenergic receptors are stimulated by the neurotransmitter **norepinephrine** (Bekdash, 2021). In addition, these primary receptors have subtypes.

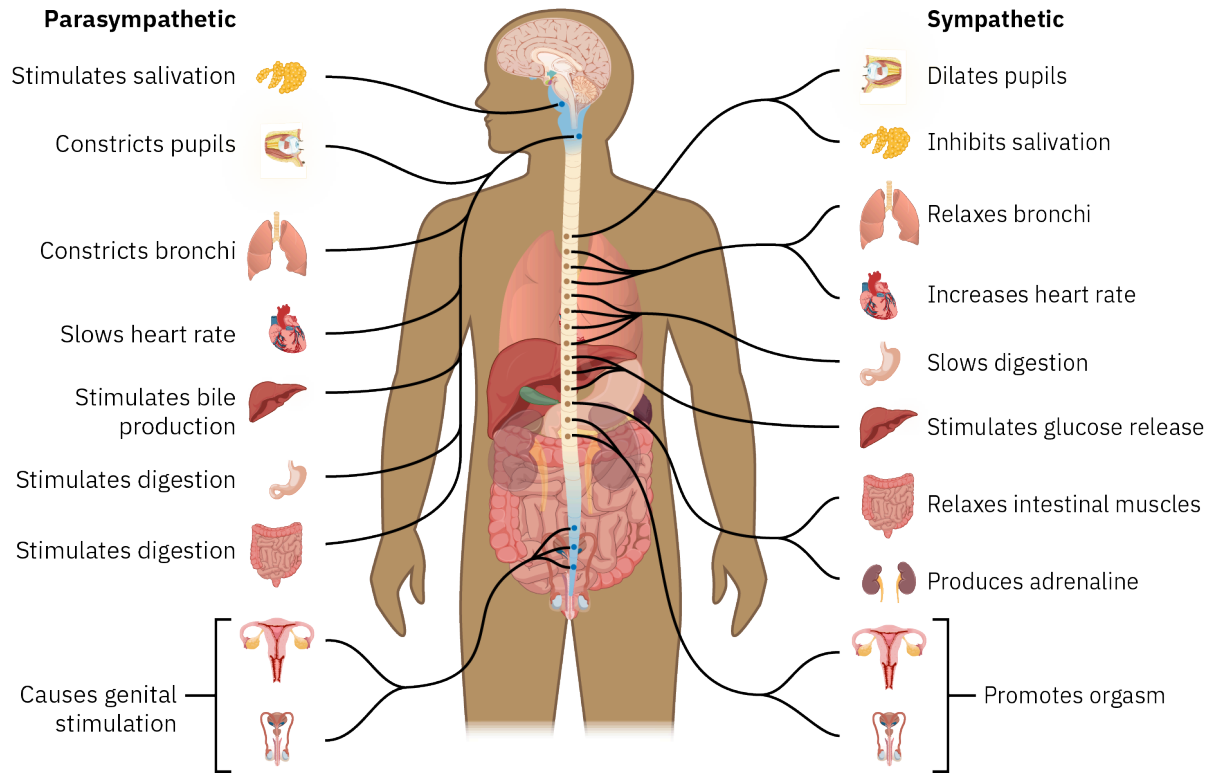


FIGURE 10.2 The autonomic nervous system consists of the parasympathetic nervous system (PSNS) and the sympathetic nervous system (SNS). The PSNS relaxes the body and maintains certain life-sustaining properties. The SNS is involved in the fight-or-flight response. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

This chapter will focus on only the cholinergic receptors with no further discussion of adrenergic receptors. There are three major subtypes of cholinergic receptors: muscarinic, nicotinic$_M$, and nicotinic$_N$. Table 10.1 describes the functions of each of these. In some organs, the PSNS and SNS work in opposition to each other (such as increasing or decreasing the heart rate). In other organs, the two systems have a complementary effect where both divisions are necessary for a physiological function to occur; for example, the PSNS is involved in males obtaining an erection, and the SNS is responsible for ejaculation. Both systems are required to work together for reproduction to successfully take place.

Notably, cholinergic receptors are not associated with the nervous system in any way. Regardless, the cholinergic receptors on blood vessels do have pharmacologic efficacy because drugs that are able to activate these receptors will cause blood pressure to decrease.

Receptor Type		Function
Muscarinic		• Promotes increased glandular secretions from pulmonary, gastric, intestinal, and sweat glands • Causes contraction of smooth muscle in the bronchi and increase bronchial secretions
Nicotinic	Muscle	• Causes contraction of skeletal muscle
	Neuronal	• Stimulates ganglionic transmission at all ganglia of the SNS and PSNS • Promotes release of epinephrine from the adrenal medulla

TABLE 10.1 Functions of Acetylcholine at Cholinergic Receptor Subtypes

10.1 Introduction to Myasthenia Gravis

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 10.1.1 Describe the pathophysiology of myasthenia gravis.
- 10.1.2 Identify the clinical manifestations related to myasthenia gravis.
- 10.1.3 Identify the etiology and diagnostic studies related to myasthenia gravis.

Myasthenia gravis (MG) is a progressive autoimmune neuromuscular disorder characterized by fluctuating muscle weakness and the onset of rapid fatigue. This disease does not discriminate based on gender, race, ethnicity, or religion—it most commonly affects young adult females (under 40) and older males (over 60), but it can occur at any age, including childhood (National Institute of Neurological Disorders and Stroke, 2023b). To date, no biological inheritance component has been associated with MG. The disease can present in two forms: ocular and generalized. The ocular form causes muscle weakness only in the eyelids and extraocular muscles. The generalized form includes a combination of extremities, esophageal and respiratory muscles, and the aforementioned ocular form.

Pathophysiology

Myasthenia gravis is an autoimmune disorder of neuromuscular junction (NMJ) transmission. In a healthy person, nerve impulses release ACh at the NMJ, the area where nerve cells connect with the muscles they control. This neurotransmitter, ACh, will then travel across the synapse, where it will reach nicotinic$_M$ receptors located on the muscle endplate. Once ACh has activated enough receptor sites, muscle contraction will occur. According to the National Institute of Neurological Disorders and Stroke (2023b), individuals with MG lack a significant number of functional receptor sites (as much as 70%–90%) because the individual's immune system produces antibodies (protein produced in response to a specific antigen) that block, alter, or destroy the receptors for acetylcholine at the NMJ. In addition to fewer receptor sites, the synaptic space widens, which impairs signal transmission. The outcome of these changes is the inability of muscles to contract, resulting in muscle weakness.

Etiology

What triggers an immunological attack on the NMJ receptor sites is not fully understood. The **autoantibodies** (antibodies that destroy a person's own proteins and antigens) against the ACh receptors have been identified as immunoglobulin G (IgG) derived from the plasma B-lymphocytes. These antibodies destroy ACh receptor sites, but they also attack other proteins such as the muscle-specific kinase (MuSK) protein that impairs the neurotransmitter's communication at the NMJ. T-lymphocytes also play a role in this immunological attack. The thymus is the principal organ in cell-mediated immunity. Normally, the thymus will begin to atrophy after puberty. Thymus abnormalities, such as hyperplasia (enlarged thymus) or thymoma (tumor on the thymus gland) have been acknowledged in those with MG. It is believed the thymus gland provides incorrect instructions to developing immune cells, which results in the immune system not recognizing itself and attacking its own cells and tissues while producing acetylcholine receptor antibodies.

Diagnostics

Because weakness is a common and vague complaint, diagnosis of MG can be delayed or even missed. Several different tests can be conducted to confirm the diagnosis of MG. Just like with most conditions, the nurse should first obtain an accurate history and physical examination. The assessment of the neurological system is the primary focus: the client's muscle strength, tone, and coordination should be examined; sensation and extraocular eye movements should be evaluated.

Serological tests can detect the presence of anti-ACh receptor antibodies and/or anti-MuSK antibodies circulating within the bloodstream. However, some clients with MG will have neither of these antibodies, a condition termed seronegative (negative antibody) myasthenia gravis.

A single-fiber electromyography (EMG) test can detect delayed or failed neuromuscular transmission in muscle fibers that are supplied by a single nerve fiber. The EMG is considered the most sensitive test in diagnosing MG. Another noninvasive examination is the repeated nerve stimulation test, which stimulates the nerves with small pulses of electricity for the purpose of tiring specific muscles. Muscle fibers in myasthenia gravis do not respond well to repeated electrical stimulation. To confirm a thymoma or enlarged thymus, a computed tomography (CT) or

magnetic resonance imaging (MRI) test is performed.

Clinical Manifestations

Ptosis (drooping of the eyelid) and **diplopia** (double vision) are the presenting symptoms in half of the clients diagnosed with MG. The cardinal feature of early MG is fluctuating skeletal muscle weakness and muscle fatigue. Many times, muscle strength is strongest in the morning hours and will decrease throughout the day. The fatigue is an indication there is worsening of the muscle contractile force, most notably seen with repetitive motions, such as blinking, walking, or even talking. For instance, a client's speech may become slurred after a few minutes of constant talking. This is referred to as **dysarthria** (difficulty speaking). After resting, the voice will return to baseline, and speech will become clear. As the disease progresses, muscle weakness and fatigue become more constant.

Several factors can exacerbate MG symptoms, including emotional stress, infection, surgery, aminoglycosides, hypo- or hyperthyroidism, hormonal fluctuations, and an increase in body temperature. A sudden exacerbation of symptoms is known as a myasthenic crisis, which is considered a medical emergency because fatal consequences can result. If respiratory muscles are affected, ventilation will be compromised. Chewing and/or swallowing muscles can also be affected because the disease eventually affects the muscles of the lower half of the face. The impairment of these muscles will result in **dysphagia** (difficulty swallowing) and lead to choking and/or aspiration.

Pharmacological Management

The main pharmacological class to treat MG is acetylcholinesterase (AChE) inhibitors. These indirect-acting cholinergic agonists react chemically with AChE, the enzyme responsible for breaking down ACh in the synaptic cleft. The presynaptic neuron continues to release ACh, while the synapse accumulates ACh because it is not broken down. This results in the cholinergic receptors being stimulated for a prolonged period of time. The reversible AChE inhibitors are used to treat MG because they are effective at all the cholinergic junctions (muscarinic, ganglionic, and neuromuscular).

Some cases of MG may go into **remission** (resolution of symptoms), either temporarily or permanently, where muscle weakness disappears completely. Drugs may not be needed during these periods. When the MG is well controlled, the safety factor of nerve to muscle transmission has been largely restored, and strength has been increased. In contrast, when clients still have symptoms with first-line agents, they may require immunosuppressive therapy, which may include high-dose glucocorticoids, until symptoms are under control. These drugs cause lysis of antigen-activated lymphocytes, suppress lymphocyte proliferation, and increase sequestration of lymphocytes at extravascular locations. The doses for immunosuppressive purposes are high, leading to a broad spectrum of adverse effects. When the client's symptoms are under control, the glucocorticoids should be gradually titrated and discontinued.

Other immunosuppressants and immunomodulators are also used when MG is not well-controlled. One example of an immunosuppressant is azathioprine. This drug blocks the purine pathway and inhibits DNA, RNA, and protein synthesis, which causes the immune system to be unable to mount a response to an antigen. Azathioprine is given orally. It does have a black box warning related to the risk of malignancy (DailyMed, *Azathioprine*, 2022). Immunomodulators can deliver more targeted drug therapy. These are also known as monoclonal antibodies (MABs). Overall, these drugs activate the body's natural immune response. For a more detailed discussion of these classifications, please refer to Drugs to Treat Parkinson's Disease and Multiple Sclerosis.

LINK TO LEARNING

Living with Myasthenia Gravis

Access multimedia content (https://openstax.org/books/pharmacology/pages/10-1-introduction-to-myasthenia-gravis)

This educational video, "Behind the Mystery: Myasthenia Gravis," shares the story of a client who lives with MG. In addition, University of South Florida Health Department of Neurology physician Dr. Niraja Suresh discusses the cause and progression of the disease, how a diagnosis is confirmed, and managing the disease.

10.2 Cholinergic Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 10.2.1 Identify the characteristics of drugs used to treat myasthenia gravis.
- 10.2.2 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat myasthenia gravis.
- 10.2.3 Describe nursing implications of drugs used to treat myasthenia gravis.
- 10.2.4 Explain the client education related to drugs used to treat myasthenia gravis.

Cholinergic agonists are also termed **parasympathomimetics**, and cholinergic antagonists (also known as anticholinergics) are termed **parasympatholytics**. (The anticholinergic agents will be discussed in Drugs to Treat Parkinson's Disease and Multiple Sclerosis.) The PSNS has two general sites where drugs can act: (1) the synapses between **preganglionic neurons** and **postganglionic neurons**, and (2) the junctions between postganglionic neurons and their effector organs. The class of cholinergic agonists is subdivided into direct acting and indirect acting. The direct-acting cholinergic agonists interact with the postsynaptic cholinergic receptors and cause them to perform the same functions as if endogenous ACh was present. The indirect-acting cholinergic agonists are classified as AChE inhibitors and do not bind directly to receptors. AChE inhibitors prevent the enzyme from destroying acetylcholine. Because the enzyme is inhibited, there is more acetylcholine available for use. AChE inhibitors are subdivided into two categories: reversible and irreversible. These classes are discussed in the following sections.

Direct-Acting Cholinergic Agonists

Direct-acting cholinergic agonists mimic the effects of ACh when they bind to cholinergic receptors. They are considered direct acting because they have **affinity** (attracted to a receptor) and **intrinsic activity** (ability to stimulate a receptor) to these receptors. Direct-acting cholinergic agonists mainly bind to the muscarinic receptors of the PSNS. (Refer to Table 10.1 earlier in this chapter to see responses produced when muscarinic receptors are activated.) The most common therapeutic uses for these drugs are to promote urinary excretion and gastrointestinal (GI) motility/secretions. Additionally, there are several direct-acting cholinergic agonists that are found in ophthalmic formulations and induce miosis for the purpose of treating glaucoma because they help to relieve increased intraocular pressure. An example of a direct-acting cholinergic agonist in an ophthalmic formulation is pilocarpine. Pilocarpine also comes as an oral solution and is used to treat dry mouth associated with Sjogren's syndrome or salivary gland damage. Due to the direct-acting cholinergic agonist's selective action on muscarinic receptors, nicotinic responses are minimal or nonexistent; therefore, this class is not used in the treatment of MG.

Indirect-Acting Cholinergic Agonists: Reversible Acetylcholinesterase Inhibitors

Indirect-acting cholinergic agonists bind reversibly to AChE. They inhibit the enzyme that destroys acetylcholine, making acetylcholine more available. The specific mechanism of action is to delay the splitting of ACh into choline and acetone. Because AChE must degrade the drug in order to become unbound, less of this enzyme is available to break down ACh. This leaves more ACh to bind to the cholinergic receptors, intensifying its response at all the junctions where it serves as the neurotransmitter. The result of this action is prolonging access to ACh, allowing it to accumulate within the synaptic cleft; ACh continues binding to cholinergic receptors on the postsynaptic neuron, causing activation of that neuron. The effectiveness lasts until AChE is released. Once released, AChE will begin to break down ACh, and the effects of the drug will wear off. Reversible inhibitors produce effects of moderate duration. The optimal dose is determined by administering a small initial dose followed by gradual small increases until optimal muscle function is observed.

Pyridostigmine Bromide

Pyridostigmine bromide is the drug of choice for managing MG. This drug is formulated in a powder, syrup, or tablet. Tablets are available in immediate-release (IR) and extended-release (ER) forms. Both IR and ER forms may be needed to sustain effects. When adequate amounts of ACh are present at the NMJ, skeletal muscle is stimulated. The force of skeletal muscle contraction is increased at therapeutic doses. In contrast, too much drug can reduce the force of skeletal muscle strength because it leaves the NMJ in a state of constant depolarization.

Neostigmine

Neostigmine is administered only intravenously (IV). Essentially, it is used in the diagnosis and treatment of MG and reversal/recovery of the nondepolarizing neuromuscular blocking agents after surgery. The onset of action is 10–30 minutes, and peak effects occur in 20–30 minutes. Atropine should be readily available when infusing this drug.

A peripheral nerve stimulation device (also known as a train of four) is used to determine the degree of muscle relaxation based on muscle response after a stimulus is provided. This helps to determine if more medication is necessary when reversing any neuromuscular blockade postoperatively. The train of four count consists of four consecutive 2-Hz stimuli to a muscle group and the number of twitches evoked.

Table 10.2 lists common reversible AChE inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Pyridostigmine bromide (Mestinon)	Highly individualized. *IR dosage range*: 60–1500 mg orally daily; typical dose is 600 mg daily divided into 5 doses. *ER dosage range*: 180–540 mg orally daily or twice daily.
Neostigmine (Bloxiverz)	*Diagnosis of MG:* 0.022 mg/kg intramuscularly. *Reversal of nondepolarizing neuromuscular blocking agents:* Dose is individualized to control symptoms: 0.03–0.07 mg/kg intravenously (IV).

TABLE 10.2 Drug Emphasis Table: Indirect-Acting Reversible Acetylcholinesterase Inhibitors (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

If the amount of pyridostigmine becomes too elevated, this can result in a cholinergic crisis. It is essential that the prescriber does not interpret skeletal muscle weakness as a sign of inadequate dosing because increasing the dose will elevate the risk of cholinergic crisis.

SAFETY ALERT

Differentiating Between Cholinergic Crisis and Myasthenic Crisis

Taking too much of an AChE inhibitor can result in cholinergic crisis. Cholinergic and myasthenic crises share similar symptoms, such as muscle weakness or paralysis. The nurse must accurately distinguish between the two because the treatments are very different. A medication history or signs of excessive cholinergic stimulation (excess saliva, watery eyes, difficulty breathing, bradycardia, frequent urge to urinate, muscle twitching, and nausea/vomiting/diarrhea) can indicate a person is experiencing a cholinergic crisis not related to the myasthenia gravis. Stop direct or indirect cholinergic agonists until muscle strength improves.

Antidote for cholinergic crisis: Atropine (selective muscarinic antagonist) blocks the muscarinic receptors, which helps to reverse most of the signs/symptoms.

Antidote for myasthenic crisis: AChE inhibitor (pyridostigmine) will increase the necessary ACh levels.

(Sources: Adeyinka & Kondamudi, 2023; Health Union, 2023)

Apart from the adverse drug reactions associated with skeletal muscle, the majority of the adverse effects relate to the excessive stimulation of the muscarinic receptors. Intravenous atropine can alleviate the muscarinic effects. The fall in cardiac output can lead to hypotension. The diaphragm can be negatively affected, causing respiratory depression that is treated by mechanical ventilation with oxygen and not with medications. Pyridostigmine can cause bradycardia and exacerbate any underlying cardiac conduction abnormalities. Due to the constriction of the bronchi, asthmatics must be closely monitored when taking AChE inhibitors. Dysphonia (hoarseness) is the result of laryngospasms. Depending on the severity of the vomiting, diarrhea, diaphoresis, and urine output, dehydration can result.

Succinylcholine is a depolarizing neuromuscular blocker. Reversible AChE inhibitors decrease the breakdown of this

drug; therefore, this combination can intensify the neuromuscular blockade. On the other hand, atropine can negate the effects of the AChE inhibitors.

Table 10.3 is a drug prototype table for indirect-acting reversible AChE inhibitors featuring pyridostigmine bromide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Reversible AChE inhibitor **Mechanism of Action** Causes reversible inhibition of AChE within the synapse, allowing more ACh to bind to cholinergic receptors and prolonging its effects	**Drug Dosage** Highly individualized. *IR dosage range*: 60–1500 mg orally daily; typical dose is 600 mg daily divided into 5 doses. *ER dosage range*: 180–540 mg orally daily or twice daily.
Indications Management of MG symptoms Reversal of competitive (nondepolarizing) neuromuscular blockade Prevention/treatment of urinary retention in postoperative clients **Therapeutic Effects** Improves transmission of nerve impulses across the NMJ, increasing muscle strength and decreasing difficulty with chewing, swallowing, and speech, along with improvement or absence of ptosis Treats overdose from a competitive neuromuscular blocker	**Drug Interactions** Succinylcholine Atropine **Food Interactions** No significant interactions
Adverse Effects Excess salivation and lacrimation Increased urination Diaphoresis Diarrhea Nausea/vomiting Bradycardia Decrease in cardiac output Bronchospasms Dysphagia Dysarthria Dysphonia Seizures Miosis Weakness, fasciculations, or paralysis of skeletal muscles	**Contraindications** Mechanical obstruction of the intestine or urinary tract Caution: Bronchial asthma Cardiac conduction abnormalities, such as atrioventricular block

TABLE 10.3 **Drug Prototype Table: Pyridostigmine Bromide** (source: https://dailymed.nlm.nih.gov/dailymed/)

CLINICAL TIP

Underdosing Versus Overdosing

Although failure of clients to show clinical improvement may reflect underdosage, it can also be indicative of overdosage. As is true of all cholinergic drugs, overdosage of pyridostigmine bromide may result in cholinergic crisis.

Nursing Implications

The nurse should do the following for clients who are taking an indirect-acting reversible AChE inhibitor:

- Monitor heart rate/rhythm and blood pressure periodically.
- Assess respiratory pattern (rate, depth, rhythm, effort) and airway patency.
- Time the administration of the drug so that peak effects occur at meals to help with eating and swallowing.
- Evaluate client's ability to chew and swallow.
- Monitor client's ease of ability to raise the eyelids (important sign of improvement).
- Monitor for clinical manifestations of dehydration if vomiting, diarrhea, or diaphoresis is present.
- Administer antiemetics to reduce nausea and vomiting.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an indirect-acting reversible AChE inhibitor should:

- Understand that MG is not curable, so treatment is lifelong.
- Be able to recognize signs of therapeutic failure (ptosis, difficulty swallowing) and toxicity (excess muscarinic responses).
- Maintain records of the times the drug was administered, times at which fatigue occurred, and level of muscle strength before and after taking the drug.
- Wear a medic alert bracelet due to the potential of experiencing a crisis (myasthenic or cholinergic).
- Move and change positions slowly due to hypotension.
- Sit or lie down if dizziness occurs and wait until it subsides before standing or walking.
- Ensure adequate lighting to enhance vision due to the pupillary constriction.
- Ensure they have ready access to a restroom/commode due to the stimulatory effect on the GI and genitourinary (GU) systems.
- Contact their prescriber immediately if they have any difficulty with swallowing, speaking, hoarseness, or breathing.
- Space activities to obtain optimal benefit from the drug.

The client taking an indirect-acting reversible AChE inhibitor *should not:*

- Chew, break, or crush extended-release capsules.
- Rise or change positions quickly due to possible orthostatic hypotension.
- Stop drugs abruptly because symptoms will quickly reoccur.
- Overexert themselves; they should take rest periods between activities.

Indirect-Acting Cholinergic Agonists: Irreversible AChE Inhibitors

These drugs bind irreversibly to AChE. The effects of these drugs are prolonged—they will last until new molecules of cholinesterase are synthesized. Another method of reversing the inhibition of AChE, especially at the NMJ, is to administer pralidoxime, a cholinesterase reactivator. This drug is a specific antidote to poisoning by the irreversible cholinesterase inhibitor. The drug has no effect on reversible AChE inhibitors. This medication is administered either via IV or intramuscularly. Dosage is individualized according to the severity of symptoms.

The only *therapeutic* indication for this drug class is the treatment of glaucoma. For that indication, only one drug, echothiopate, is available. The drugs have limited use because they are highly toxic. Once they become absorbed, they will easily cross the blood–brain barrier, causing adverse effects.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Rae Lennon is a 38-year-old assistant professor at a small university. In November, they noticed that their vision was blurry, especially when grading papers. Rae said that they were seeing double. At first, they just assumed they were tired because their sleeping pattern had changed over the past 2 weeks and they were not getting enough sleep.

About a month after that, while drying their hair, Rae observed their left eyelid was drooping and it was becoming difficult to hold the hairdryer due to weakness in the arms. Over the Christmas break, Rae visited the primary care provider, who referred Rae to a local neurologist based on the symptoms. During Rae's appointment with the neurologist, a thorough history and physical assessment were carried out. In addition, blood tests results revealed elevated levels of acetylcholine receptor antibodies. Based on these results, Rae was diagnosed with MG.

History
Overactive bladder

Current Medications
Oxybutynin 5 mg, 4 times daily

Vital Signs		Physical Examination
Temperature:	98.2°F	• *Head, eyes, ears, nose, and throat (HEENT):* Normocephalic, left eyelid droop, minimal facial expressions. Ears, nose, and throat unremarkable. Vision 20/25 in both eyes via Snellen chart. Near vision poor using Rosenbaum card. • *Cardiovascular:* Audible S1, S2. Rhythm regular. No murmurs, rubs, or gallops. No peripheral edema bilaterally. Radial and dorsalis pedis pulses 2+. • *Respiratory:* Lungs clear bilaterally in all fields. • *GI:* Abdomen round, soft, and nontender. Bowel sounds present in all four quadrants. • *Musculoskeletal:* Limited range of movement (ROM) in bilateral upper extremities and 3/5 muscle strength. Lower extremities with full ROM and 5/5 muscle strength.
Heart rate:	72 beats/min	
Respiratory rate:	18 breaths/min	
Blood pressure:	112/64 mm Hg	
Oxygen saturation:	96% on room air	
Height:	5'6"	
Weight:	138 lb	

TABLE 10.4

1. Which class of medication will the neurologist prescribe Rae to improve their symptoms?
    a. Cholinergic agonist
    b. Cholinergic antagonist
    c. Indirect-acting reversible cholinesterase inhibitor
    d. Indirect-acting irreversible cholinesterase inhibitor

2. What is the main cause of this disease?
    a. Abnormal tau protein and neurofibrillary tangles
    b. Antibodies attacking the nicotinic$_N$ receptors
    c. Beta-amyloid plaques and oxidative stress
    d. Destruction of the myelin sheath

TRENDING TODAY

A New Medication for Myasthenia Gravis

The U.S. Food and Drug Administration (FDA) has approved a new medication, rozanolixizumab-noli (Rystiggo), for generalized MG in adults who are anti-acetylcholine receptor (AChR) or anti-MuSK antibody positive, the two most common subtypes of generalized MG. Rozanolixizumab-noli is a humanized IgG4 monoclonal antibody that is administered through a weekly subcutaneous infusion. A 6-week treatment cycle study has shown rapid

improvement in clients' activities of daily living (DailyMed, *Rystiggo*, 2023). Significant adverse effects include the increased risk of infection, aseptic meningitis, and hypersensitivity reactions, such as rash and angioedema. It is contraindicated in those with an active infection and should not be started until the infection is resolved (Source: DailyMed, *Rystiggo*, 2023).

10.3 Introduction to Alzheimer's Disease

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 10.3.1 Describe the pathophysiology of Alzheimer's disease.
- 10.3.2 Identify the clinical manifestations related to Alzheimer's disease.
- 10.3.3 Identify the etiology and diagnostic studies related to Alzheimer's disease.

Alzheimer's disease (AD) is the most common neurodegenerative condition of the brain and is characterized by significant changes in brain tissue. This disease is the most frequent cause of dementia in older adults. It is estimated that nearly 13 million Americans age 65 and older will develop AD and other dementias by 2050, according to the 2023 Alzheimer's Association Disease Facts and Figures report (https://openstax.org/r/alzorgnews). Alzheimer's is irreversible and eventually has a major negative impact on cognition due to loss of short-term memory, reasoning, insight, and judgment and the inability to learn new information. It also has an undesirable effect on a client's social functioning skills. However, the disease progresses very slowly; the risk of AD increases with age, but it can also occur between the ages of 30 and the early 60s (National Institute of Neurological Disorders and Stroke, 2023a).

Several factors have been identified that may reduce the risk of AD. These include higher levels of formal education, routinely engaging in mentally challenging activities—such as reading—adequate uninterrupted deep sleep, engaging in routine aerobic exercise, eating a healthy balanced diet, and maintaining social interactions.

Two major goals of care are maintaining socialization and providing support for caregivers. One way to provide relief for caregivers while increasing socialization for clients is adult daycare and respite centers.

LINK TO LEARNING

Alzheimer's Prevention

Access multimedia content (https://openstax.org/books/pharmacology/pages/10-3-introduction-to-alzheimers-disease)
In this TEDx Talk, entitled "What You Can Do to Prevent Alzheimer's," neuroscientist Lisa Genova describes the pathophysiology of the disease, with an emphasis on ways to potentially prevent the disease. Her presentation also discusses the concept of neuroplasticity and building a resistance to the changes in the brain seen with AD.

Access multimedia content (https://openstax.org/books/pharmacology/pages/10-3-introduction-to-alzheimers-disease)
This video, also featuring Lisa Genova, explains that most forgetfulness in aging is normal. It also describes five ways to build an Alzheimer's-resistant brain.

Pathophysiology

To fully understand how a drug alters symptoms, it is important to understand the pathophysiology of the disease being treated at the biochemical level. In most central nervous system disorders, the existing knowledge is limited. The brain is a complex structure, and the overall neuronal degeneration and cerebral atrophy recognized in AD has been theorized to result from a variety of changes. Researchers are still trying to unravel the underlying pathophysiology of AD. The following is a list of alterations that have been identified as origins for the cognitive decline seen with this disease (Huang, 2023):

- *Degeneration of neurons:* This destruction of neurons first occurs in the hippocampus, the area of the brain that plays an essential role in memory. The degeneration of these neurons will cause short-term memory loss.

When neurons of the cerebral cortex begin to degenerate, speech, reasoning, and other higher cognitive functions become impaired.

- *Beta-amyloid plaques:* These plaques form outside neurons. Their central core is composed of beta-amyloid, a protein fragment of amyloid precursor protein (APP). Accumulation of beta-amyloid begins very early in the disease before any appearance of clinical manifestations. It is believed this protein plays a central role in AD.
- *Neurofibrillary tangles and abnormal tau protein:* These tangles form inside neurons. They result when the orderly arrangement of **microtubules** becomes disrupted. Microtubules are responsible for bringing nutrients to the axons and back. Normally, tau protein binds to these microtubules and provides stability. In AD, tau protein becomes "sticky" and tangles together with other tau threads. The microtubule is unable to transport nutrients, so the neuron can no longer function and eventually dies. As more and more neurons die, the brain atrophies.
- *Oxidative stress:* Oxidative stress produces reactive oxygen species (ROS), such as free radicals. These cause brain cell damage and cellular **apoptosis**. *Oxidative stress* is the term used to describe damage to cellular components caused by ROS. Due to their characteristic unpaired electrons, ROS can set off chain reactions where they remove electrons from other molecules, which then become oxidized and reactive and do the same to other molecules, causing a chain reaction. ROS can cause permanent damage to cellular lipids, proteins, carbohydrates, and nucleic acids. Damaged DNA can lead to genetic mutations and even cancer.
- *Deficiency of ACh:* The loss of ACh is crucial for two reasons: (1) it is an important transmitter in the hippocampus and cerebral cortex, where the degeneration is occurring; and (2) this transmitter is critical in forming memories.
- *Genetics:* Apolipoprotein E is known for its role in transporting cholesterol. One form of apolipoprotein E is associated with AD. Genetic research has shown that those with one or two copies of the gene that codes for apolipoprotein E4 (APOE-e4) are at a higher risk for developing AD. Additional genes have been identified as being definitively associated with AD. These include amyloid precursor protein (APP) gene, presenilin-1 (PS1) gene, and presenilin-2 (PS2) gene. A person who has any mutation to these genes will produce proteins that have **neurotoxic** properties, which will promote neuronal death. Additionally, these mutations can lead to the formation of neurofibrillary tangles and plaques.

Etiology

An underlying single cause for AD has yet to be discovered. There have been important theories and findings, but it is not known how these pieces fit together. Interestingly, the major pathologic findings begin to develop a decade or more before clinical manifestations are even observed. At this point, the etiology is considered multifactorial. Current potential causes of AD include:

- Degeneration of neurons in the hippocampus and cerebral cortex that subsequently cause cerebral atrophy
- Formation of beta-amyloid plaques
- Accumulation of neurofibrillary tangles and chemically altered tau protein
- Oxidative stress forming free radicals that damage cellular components caused by ROS (This is discussed more in the following section.)
- Deficiency of acetylcholine
- Genetics

Figure 10.3 compares a cross-section of a normal brain with one from a client with Alzheimer's disease.

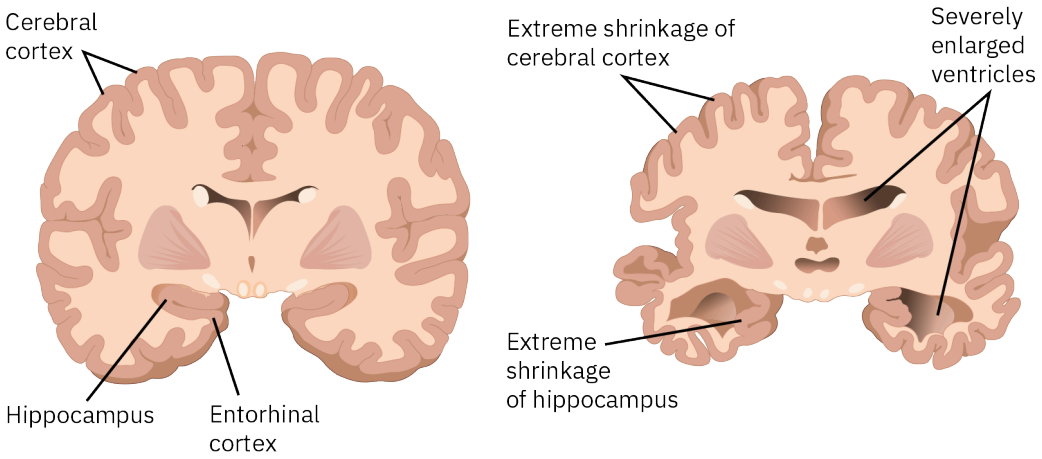


FIGURE 10.3 Compared with a normal brain (left), the brain from a client with Alzheimer's disease (right) shows a dramatic neurodegeneration, particularly within the ventricles and hippocampus. (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Diagnostics

Although it is impossible to definitively diagnose AD without a postmortem autopsy, the diagnosis is made based on symptoms and exclusion of alternative pathology. During the autopsy, the typical characteristics of senile plaques and neurofibrillary tangles can be visualized.

Clinical Manifestations

As the disease progresses, the clinical manifestations worsen to the point where the client is unable to independently perform their activities of daily living (ADL). They become reliant on others for assistance. Early in the disease, the following mild manifestations may be witnessed: confusion, memory loss, disorientation, getting lost in familiar surroundings, problems with routine tasks, and changes in personality and judgment. Moderate manifestations include difficulty with ADLs (feeding and bathing), impaired organization and planning, impaired mathematical ability, anxiety/agitation, sleep disturbances, wandering, and difficulty in recognizing family and friends. Late manifestations include loss of speech, anorexia, impaired swallowing, weight loss, difficulty with movement, loss of ability to appropriately respond to the environment, sense of paranoia, **delusions**, **hallucinations**, and inability to control bladder and bowel function. At this point, the client is completely dependent on caregivers. AD will eventually destroy enough brain function to cause death.

Pharmacological Management

Currently, there is no known cure for AD. Drugs given for AD may at best slow the loss of memory and cognition in hopes of affording the person extra time to be able to continue functioning independently. Unfortunately, often the person observes minimal and short-term clinical efficacy from these medications. The AChE inhibitors (also known as cholinesterase inhibitors) were the first class of drugs approved by the FDA to treat AD. There are currently three drugs within this class. The other drug class, which currently contains one drug, is the N-methyl-D-aspartate (NMDA) receptor antagonist. In 2014, a capsule containing a combination of memantine hydrochloride ER (NMDA receptor antagonist) and donepezil hydrochloride (AChE inhibitor) was approved for the treatment of moderate to severe dementia of the Alzheimer's type. This drug has the capability of targeting two different sites of action.

10.4 Alzheimer's Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 10.4.1 Identify the characteristics of drugs used to treat Alzheimer's disease.
- 10.4.2 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat Alzheimer's disease.
- 10.4.3 Describe nursing implications of drugs used to treat Alzheimer's disease.
- 10.4.4 Explain the client education related to drugs used to treat Alzheimer's disease.

AChE Inhibitors

AChE inhibitors bind to and interfere with the enzyme AChE. This enzyme is responsible for the destruction of ACh. By inhibiting this enzyme, more internally released ACh is available for use within cholinergic synapses. The result is enhanced transmission by central cholinergic neurons that have not yet been destroyed. Elevated ACh levels in the cortex can slow the neuronal degradation that occurs in this disease. Treatment with AChE inhibitors does not stop the progression of AD but reduces how quickly neurons are destroyed.

Donepezil

Donepezil, a centrally acting reversible cholinesterase inhibitor, is used primarily for treatment of mild to severe forms of AD. Centrally acting agents readily cross the blood–brain barrier. Donepezil increases ACh in the brain by preventing its breakdown. Drug absorption is unaffected by food. Peak effects occur in 3–8 hours. Metabolism occurs in the liver, resulting in the production of several pharmacologically active metabolites. Excretion is through the kidneys. An important pharmacokinetic note is that donepezil is highly protein bound (96%); therefore, it has a prolonged half-life of 70 hours. This means that it takes an estimated 15 days for the drug to reach **steady state**.

SAFETY ALERT

Similarly Named Drugs

Do not confuse Aricept (AChE inhibitor) with Aciphex (proton pump inhibitor).

(Source: Institute for Safe Medication Practices [ISMP], 2023)

Galantamine

Galantamine is only used in those with mild to moderate AD. The drug is prepared by extraction from daffodil bulbs. Like donepezil, this drug is a reversible inhibitor of AChE. GI effects are greater than with donepezil but less than with oral rivastigmine (see the next section). Adverse effects are the same as for donepezil with the addition of potential life-threatening skin reactions, such as **Stevens–Johnson syndrome**. Clients and caregivers should stop the drug and report any signs of a skin rash to their health care provider. As with the other AChE inhibitors, benefits of the drug are modest and short-term. The drug is available in IR and ER tablets as well as an oral solution. Its half-life is 7 hours.

Rivastigmine

Rivastigmine is FDA-approved for those with mild to severe AD because it enhances cholinergic function. The manner in which it does so is not fully known. It is believed to increase the ACh concentration by reversible inhibition of its hydrolysis by cholinesterase. Additionally, rivastigmine is used in the management of mild to moderate dementia due to Parkinson's disease. The drug is available in capsules, oral solution, and a transdermal patch. Peripheral cholinergic effects, such as nausea, vomiting, diarrhea, and anorexia, occur more frequently with this drug. Blood levels are lower when using the transdermal route; therefore, the intensity of adverse effects is decreased. The liver does not metabolize this agent, so there are no significant drug–drug interactions.

CLINICAL TIP

Rivastigmine and Weight

Rivastigmine blood levels vary with weight; careful titration and monitoring should be performed in clients with low or high body weights.

CLIENT TEACHING GUIDELINES

The client using a rivastigmine transdermal patch should:

- Apply the patch every 24 hours to clean, dry, hairless, and intact healthy skin in a place where clothes will not rub against it.

- Avoid skin areas where cream, lotion, or powder has recently been applied.
- Press down firmly for 30 seconds when applying the patch until the edges stick well.
- Use the upper or lower back as the site of application to prevent inadvertent removal. If sites on the back are not accessible, apply the patch to the upper arm or chest.
- Only wear one patch at a time. (They should remove the previous day's patch before applying a new patch). If a patch falls off or a dose is missed, they should apply a new patch immediately.
- Place used patches in the previously saved pouch and discard in the trash, away from pets or children.
- Wash hands with soap and water after removing the patch; avoid touching the eyes until hands are washed. In case of contact with eyes after handling the patch, rinse immediately with water.

The client using a rivastigmine transdermal patch *should not:*

- Use the patch if the pouch seal is broken or the patch is cut, damaged, or altered in any way.
- Apply to skin that is red, irritated, or cut.
- Use the same site for a period of 14 days.

Table 10.5 lists common AChE inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Donepezil (Aricept)	*Mild to moderate AD:* *Tablet, oral disintegrating tablet, or solution:* Initial dose: 5 mg daily at bedtime. Clients should be on 5 mg daily for 4–6 weeks before dose is increased to 10 mg daily. *Moderate to severe AD:* *Tablet, oral disintegrating tablet, or solution:* Initial dose: 10 mg orally daily. A dose of 23 mg daily can be administered once clients have been on a dose of 10 mg daily for at least 3 months.
Donepezil transdermal (Adlarity)	5–10 mg, administered on a weekly basis.
Galantamine (Razadyne)	*Tablets and solution:* Initial dose: 8 mg orally daily in the morning; increase to 16 mg daily after a minimum of 4 weeks on 8 mg daily. Dose may be increased to 24 mg daily after a minimum of 4 weeks taking 16 mg daily.
Rivastigmine (Exelon)	*Capsules and solution:* Initial dose: 1.5 mg orally twice daily; after at least 2 weeks and if well tolerated, dose can be increased. Maximum dose: 6 mg twice daily (12 mg daily). *Transdermal patch:* Initial dose: 4.6 mg daily. Increase dose only after a minimum of 4 weeks at the previous dose, but only if the previous dose has been tolerated. For mild to moderate AD, continue the effective dose of 9.5 mg daily for as long as therapeutic benefit persists. Maximum dose: 13.3 mg daily. For clients with severe AD, 13.3 mg daily is the effective dose.

TABLE 10.5 **Drug Emphasis Table: Acetylcholinesterase Inhibitors** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Many of the adverse effects caused by AChE inhibitors relate to the stimulation of the PSNS. GI effects are the most common, including nausea, vomiting, diarrhea, abdominal pain, increased salivation, and anorexia. These drugs can cause cardiac-suppressive effects, which can result in symptomatic bradycardia, heart block, and even cardiac arrest. They stimulate the contraction of the bladder muscle and relax the internal sphincter, which causes a sense of urinary urgency for the client. CNS cholinergic effects include miosis, blurred far vision, and difficulty seeing in dim light. Other CNS effects of headaches, dizziness, drowsiness, and possible seizures can also occur. AChE inhibitor drugs can also impair breathing in those with pulmonary disorders, such as asthma and chronic obstructive pulmonary disease (COPD), due to bronchoconstriction and increased bronchial secretions. Frequent monitoring of the breathing pattern is required. Clients with cardiac conduction disorders should be monitored carefully due to the suppressive effects on cardiac impulses.

Contraindications include peptic ulcer disease because these drugs increase the secretion of hydrochloric acid in the stomach, which can worsen the ulcer and potentially cause perforation and/or bleeding. Because of the stimulatory effect on the bladder and bowel, anyone with a bladder or bowel obstruction (mechanical or neurologic)

should avoid taking these drugs to reduce the risk of rupture.

Any drugs with anticholinergic effects—such as first-generation histamine-1 receptor antagonists (H1RAs), conventional antipsychotics, and tricyclic antidepressants (TCAs)—should not be used concurrently because they will reduce or block therapeutic effects of cholinergic agonists. Other parasympathomimetics can cause a synergistic effect if used concurrently. Frequent intake of nonsteroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids (steroids) can increase the risk of peptic ulcer disease. Clients taking drugs such as beta blockers (propranolol/metoprolol) or digoxin should be especially careful of significant bradycardia because they both cause negative **chronotropic** effects.

Table 10.6 is a drug prototype table for AChE inhibitors featuring donepezil. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Acetylcholinesterase inhibitor **Mechanism of Action** Causes reversible inhibition of AChE	**Drug Dosage** *Mild to moderate AD:* *Tablet, oral disintegrating tablet, or solution:* Initial dose: 5 mg daily at bedtime. Clients should be on 5 mg daily for 4–6 weeks before dose is increased to 10 mg daily. *Moderate to severe AD:* *Tablet, oral disintegrating tablet, or solution:* Initial dose: 10 mg orally daily. A dose of 23 mg daily can be administered once clients have been on a dose of 10 mg daily for at least 3 months.
Indications Mild to severe Alzheimer's disease To treat overdoses of atropine and other centrally acting anticholinergic drugs **Therapeutic Effects** Enhances cognitive function (memory, thought, reasoning)	**Drug Interactions** Anticholinergic agents First-generation H1RAs Conventional antipsychotics Tricyclic antidepressants (TCAs) Parasympathomimetics NSAIDs Beta blockers Digoxin **Food Interactions** No significant interactions
Adverse Effects Nausea/vomiting Diarrhea Anorexia Abdominal pain Insomnia Fatigue Dizziness Headache Seizures Muscle cramps Symptomatic bradycardia AV block Bronchoconstriction	**Contraindications** Active peptic ulcer disease Active GI bleeding Urinary or intestinal obstruction Hypersensitivity Caution: History of peptic ulcer disease Asthma COPD Cardiac conduction disorders

TABLE 10.6 **Drug Prototype Table: Donepezil** (source: https://dailymed.nlm.nih.gov/dailymed/)

NMDA Receptor Antagonist

Glutamate is the primary excitatory amino acid in the CNS. When glutamate binds to the NMDA receptors, it

displaces magnesium from the receptor channel and causes calcium to enter neurons, producing an excitatory effect. The brief period of calcium entry creates a signal in the learning and memory process. Glutamate will then quickly dissociate from the receptor, which permits magnesium to block the channel again. This prevents further calcium influx. If there is a pathological situation, glutamate will slowly but steadily leak from the presynaptic neuron, which prevents magnesium from reblocking the channel and allows calcium to continue entering the neuron. Too much neuronal calcium is toxic, causing neurodegeneration. In addition, excessive calcium overpowers the signal and impairs the memory and learning process.

Memantine

Memantine (Namenda, Namenda XR) is indicated for clients with moderate to severe dementia of the Alzheimer's type. This drug has been shown to exhibit neuroprotective action (slows the neurotoxicity). Memantine is an antagonist of the NMDA receptor subtype of the glutamate receptor. The drug blocks the influx of calcium when extracellular glutamate is low but permits calcium influx when extracellular glutamate is high. When the glutamate level is low, memantine can occupy the NMDA receptor channel. During this time, the level of intracellular calcium can normalize because no further calcium entry is permitted. During an action potential, a burst of glutamate is released, displacing memantine. This causes a short period of calcium influx. Because intracellular calcium is low, normal signaling of memory and learning can occur. When glutamate moves away from the receptor, memantine reblocks the channel, which stops further calcium entry.

Memantine ER has a terminal half-life of 60–80 hours; therefore, it can be prescribed once a day. In contrast, the immediate-release form is administered at 10 mg twice daily. A target dose of 5 mg twice daily is recommended in clients with severe renal impairment. This drug is predominately excreted unchanged in the urine. The drug is available in capsule form and administered orally. Any condition or drug that raises urinary pH to 8 or more can reduce drug elimination by 80% (see drug interactions and caution in Table 10.7), which will result in the accumulation of memantine within the plasma and increase the risk of adverse effects. If a client takes too much memantine, acidifying the urine with K-Phos Neutral or ascorbic acid, for example, will help promote elimination of the drug.

Table 10.7 is a drug prototype table for NMDA receptor antagonists featuring memantine ER. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class NMDA receptor antagonist **Mechanism of Action** Binds to the NMDA receptor to prevent the central channel from opening, which regulates the influx of calcium and slows intracellular calcium accumulation	**Drug Dosage** Starting dose: 7 mg daily; maximum maintenance dose: 28 mg daily. The dose is increased weekly by 7 mg daily until maximum dose is reached.
Indications Moderate to severe dementia of the Alzheimer's type **Therapeutic Effects** Improves memory and reduces dementia Slows the rate of clinical progression of AD	**Drug Interactions** Carbonic anhydrase inhibitors Sodium bicarbonate Thiazide diuretics **Food Interactions** No significant interactions
Adverse Effects Diarrhea/constipation Dizziness Headache Confusion Pancreatitis Hepatitis Stevens–Johnson syndrome	**Contraindications** Hypersensitivity Caution: Severe renal impairment Severe hepatic impairment Conditions that raise urine pH can cause a decreased drug elimination of memantine

TABLE 10.7 **Drug Prototype Table: Memantine** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Similarly Named Drugs

Do not confuse memantine (NMDA receptor antagonist) with methadone (full opioid agonist).

(Source: ISMP, 2023)

AChE Inhibitor/NMDA Receptor Antagonist

This is a fixed combination dose of a cholinesterase inhibitor and an NMDA receptor antagonist (Namzaric). The agent combines donepezil and memantine. Combining these drugs can be beneficial because each drug has a different mechanism of action. The cholinesterase inhibitors address the cholinergic defect, and the NMDA receptor antagonist reduces the abnormally high levels of glutamate. Essentially, the two agents confer independent benefits, and they act synergistically to enhance each other's effects.

This is an extended-release oral agent that is administered to clients with moderate to severe AD. The combination form is for those who are stabilized on 10 mg of donepezil daily but not taking memantine. Initial dose of memantine ER is 7 mg combined with donepezil 10 mg daily at bedtime. The dose can be increased weekly with a maintenance dose of memantine ER 28 mg and donepezil 10 mg daily. The nurse must monitor the client's mental status and ability to perform activities of daily living (DailyMed, *Namzaric*, 2019).

Nursing Implications

The nurse should do the following for clients receiving medications for AD:

- Emphasize that treatment is not a cure and will not reverse signs or symptoms and usually will only produce modest benefits.
- Obtain baseline data, such as orientation, mood/affect, and ability to carry out activities of daily living.
- Assess client's presence of bowel sounds, urine output, muscle strength, and mental status.
- Assess blood pressure, heart rate, electrocardiogram, respiratory status, and changes in urine and bowel elimination.
- Evaluate the client's ability to swallow with ease and speech pattern.
- Administer antiemetics to reduce nausea and vomiting.
- Monitor client's therapeutic response to the drug, such as improved memory and mood stabilization.
- Monitor renal and liver function periodically because this can alter the metabolism and elimination of the drugs.
- Ensure that caregivers are provided additional resources to help cope with the disease of their loved one.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a drug for AD should:

- Take ER capsules whole.
- When taking an oral disintegrating tablet, allow medication to dissolve completely on the tongue and follow with water.
- Prevent possible falls due to dizziness (remove clutter and rugs, have adequate lighting, use walking devices, etc.).
- Ensure they have ready access to restroom/commode due to the stimulatory effect on the GI and GU systems.
- Take medication with food to decrease gastric irritation.
- Understand GI upset is usually temporary and will subside over time.
- Contact their health care provider immediately if there is any difficulty with swallowing, speaking, breathing, or increased memory loss or agitation occurs.

- Report severe nausea, vomiting, diarrhea, anorexia, weight loss, dehydration, or signs of GI bleeding.
- Take donepezil at bedtime.
- Know how to manage and cope with emotional outbursts.
- Assess for any skin rashes and notify the health care provider instantly if observed.

The client taking a drug for AD *should not:*

- Chew, break, or crush ER capsules.
- Rise or change positions quickly due to possible orthostatic hypotension.
- Stop drugs abruptly because symptoms will quickly reoccur.
- If a dose of medication is missed, do not double up on the next dose—take the next dose as scheduled.

TRENDING TODAY

Intravenous Alzheimer's Disease Treatment

In July 2023, a new intravenous medication, lecanemab-irmb (LEQEMBI), received full FDA approval as a treatment for the mild dementia stage of Alzheimer's disease. The classification of this medication is an amyloid beta-directed antibody. The drug works by targeting harmful amyloid proteins and reducing existing amyloid plaque within the brain. An 18-month study was conducted with a sample of 1,795 people ages 50–90 years. The sample was diverse and included individuals from different ethnic and racial backgrounds who were diagnosed with mild cognitive impairment. This study concluded that treatment with lecanemab-irmb slows the progression of early AD. The drug helped improve participants' memory as well as their ability solve problems and complete daily activities. Overall, the medication's main goal is to increase the duration of independence in those with AD. Amyloid-related abnormalities are indicated by a temporary swelling in specific areas of the brain. This is seen using imaging studies. This usually resolves over time. Additional adverse effects may include an allergic reaction, angioedema, or an infusion-related reaction, such as fever, palpitations, dizziness, and/or shortness of breath. To reduce this effect, an individual may be pretreated with antihistamines, anti-inflammatories, or steroids (Eisai, 2023).

Chapter Summary

This chapter discussed the disease processes and drug classifications used in managing two irreversible neurodegenerative conditions: myasthenia gravis and Alzheimer's disease. With one exception, the drug classifications used in both diseases—direct- and indirect-acting cholinergic agonists and AChE inhibitors—essentially make more ACh available for use by the body. The increase in ACh is important for these diseases due to the degeneration of neurons that release ACh, which leads to a deficiency in this neurotransmitter. The NMDA receptor antagonists are the exception to this. This drug class prevents excess calcium influx into the cell, which can cause toxicity and cellular death. Although the medications used will not cure these diseases, they can help with symptom improvement and possibly delay progression of the disease. This allows the client to remain independent in performing their ADLs.

Key Terms

acetylcholine (ACh) major neurotransmitter of the cholinergic system
adrenergic receptors mediate responses to epinephrine and norepinephrine; include alpha and beta receptors
affinity strength of the attraction between a drug and its receptor
Alzheimer's disease (AD) most common neurodegenerative condition of the brain; characterized by significant changes in brain tissue
apoptosis programmed cell death prompted by a signal and designed to replace old cells with new ones
autoantibodies produced by the immune system and are directed against one or more of the individual's own cells, tissues, and proteins instead of foreign invaders
cholinergic receptors mediate responses to acetylcholine; include muscarinic and nicotinic receptors
chronotropic the increase or decrease of the heart rate
delusions false, fixed beliefs not shared by others
diplopia double vision—seeing two images of a single object
dysarthria difficulty speaking because of muscle weakness
dysphagia difficulty swallowing
hallucinations perceiving something to be real in the absence of actual stimuli (visual, auditory, olfactory, gustatory, or tactile)
intrinsic activity ability of a drug to activate a receptor upon binding
microtubules components of a cell skeleton that provide structure and shape to cells, facilitate cell movement and cell division, and transport nutrients/substances within cells
myasthenia gravis (MG) a progressive autoimmune neuromuscular disorder characterized by fluctuating muscle weakness and the onset of rapid fatigue
neurotoxic drugs that alter the proper functioning of the nervous system
norepinephrine neurotransmitter released by almost all of the postganglionic neurons of the SNS
parasympathetic nervous system (PSNS) a division of the autonomic nervous system that carries the predominant tone in most organs with the exception of the blood vessels; responsible for the rest and digest functions
parasympatholytic drugs that oppose the effects of the parasympathetic nervous system (also known as anticholinergic action)
parasympathomimetic medications that activate the parasympathetic nervous system by mimicking the effects of acetylcholine
postganglionic neuron neuron that goes from the ganglia to effector organs
preganglionic neuron neuron that goes from the spinal cord to the ganglia and releases neurotransmitters
ptosis drooping of the upper eyelid
remission disappearance of the signs and symptoms of a disease
steady state amount of drug eliminated equals the amount of drug within the circulation
Stevens-Johnson syndrome hypersensitivity response to certain drugs characterized by lesions of the skin and mucous membranes, fever, malaise, and toxemia
sympathetic nervous system (SNS) a division of the autonomic nervous system that is responsible for the fight-or-flight response

Review Questions

1. Donepezil is an acetylcholinesterase (AChE) inhibitor. Which of the following is consistent with the action of this drug?

a. The drug is used to treat mild and severe forms of Alzheimer's disease.
b. The drug cannot cross the blood–brain barrier.
c. The drug must be taken 30 minutes before meals.
d. The drug requires twice-daily dosing due to a short half-life.

2. In Alzheimer's disease, which pharmacologic action within the brain will reduce the symptoms seen with this progressive disease?
a. Decreased sensitivity of cholinergic receptors on the postsynaptic neuron
b. Decreased action of acetylcholinesterase (AChE)
c. Inhibition of the release of acetylcholine (ACh) from presynaptic neurons
d. Increased amount of available acetylcholinesterase (AChE)

3. A nurse is teaching a 74-year-old client how to properly apply a rivastigmine transdermal patch. Which of the following statements from the client requires additional teaching?
a. "The patch needs to be changed weekly."
b. "I should apply the patch over a clean, hairless, and intact area of the skin."
c. "The old patch must be removed before a new patch is put on."
d. "Sites should be rotated and the same site should not be used for 14 days."

4. The client asks the nurse how the drug memantine works in the body. What is the nurse's best response to the client's question?
a. "It inhibits the cholinesterase enzyme so that less ACh will be broken down into choline and acetone."
b. "The drug binds to the magnesium site on the glutamate receptor to slow calcium influx into the cell."
c. "The drug binds directly to the cholinergic receptors and blocks calcium from entering the cell."
d. "It will bind directly to the centrally acting muscarinic receptors to enhance cognitive function."

5. A client taking donepezil has been prescribed a new drug. Which drug prescription should the nurse question?
a. Second-generation H1RAs
b. Acetaminophen
c. Propranolol
d. Selective serotonin reuptake inhibitors (SSRIs)

6. Which AChE inhibitor should be stopped immediately if the client notices a rash?
a. Donepezil
b. Galantamine
c. Pyridostigmine
d. Neostigmine

7. A client has just been diagnosed with mild Alzheimer's disease. The health care provider prescribes donepezil oral disintegrating tablet 5 mg daily. What key point should the client be taught about how to take this drug?
a. "You may crush the pill and mix with food if you have problems swallowing the whole pill."
b. "This medication should only be taken in the morning with your breakfast."
c. "Allow the drug to completely dissolve on your tongue. Do not swallow it whole."
d. "The drug is soft enough that you can chew it if you are afraid of choking."

8. What indicates an optimal dosage of acetylcholinesterase (AChE) inhibitors for clients with myasthenia gravis?
a. Muscle relaxation
b. Pupil constriction
c. Increased intestinal motility
d. Increased ability to raise eyelids

9. The nurse is assigned to a client with a diagnosis of myasthenia gravis. The client was taking pyridostigmine 1000 mg daily. Due to the exacerbation of their symptoms, the provider increased the dose to 1500 mg daily. What condition should the nurse be assessing?

a. Sinus tachycardia
b. Hypertension
c. Fluid volume deficit
d. Fluid volume overload

10. The nurse should be prepared to administer which drug to a client experiencing a cholinergic drug overdose?

a. Epinephrine
b. Atropine
c. Propranolol
d. Pilocarpine

CHAPTER 11

Drugs to Treat Parkinson's Disease and Multiple Sclerosis

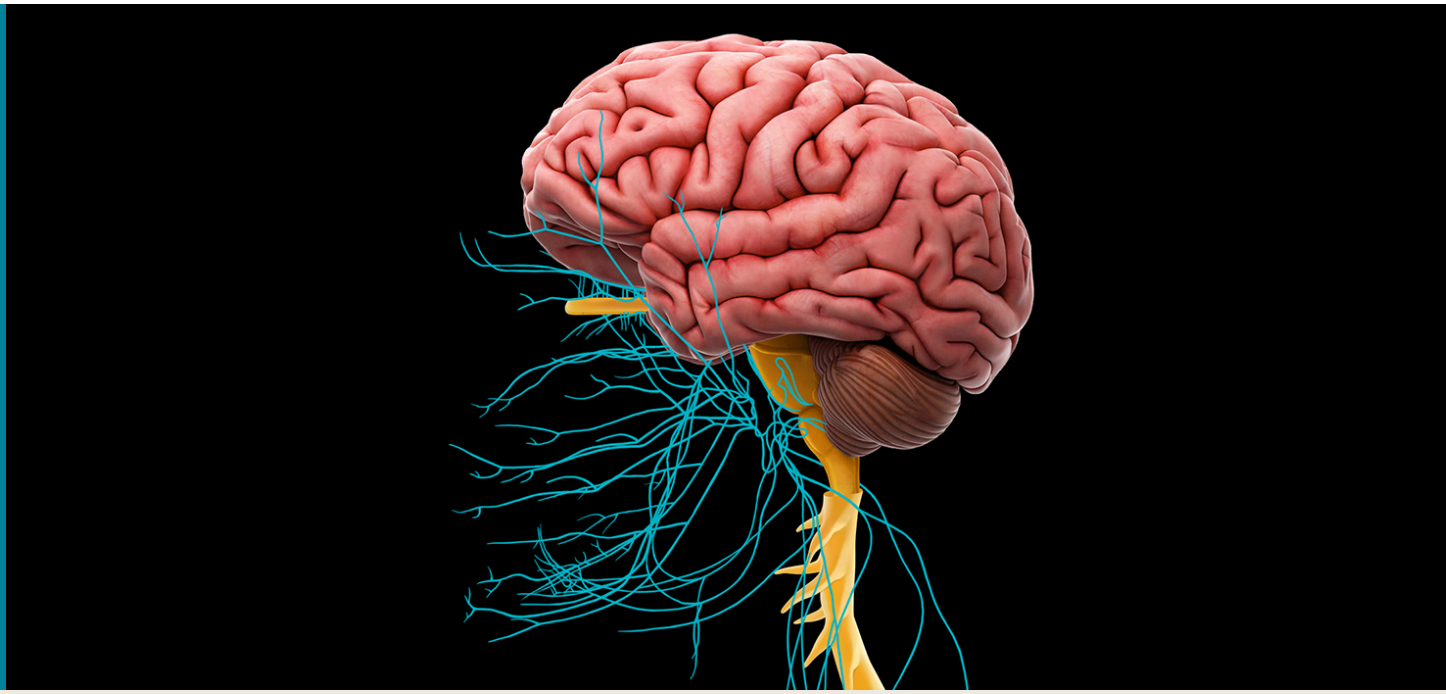


FIGURE 11.1 The nervous system, the body's control center, consists of the brain, the spinal cord, and a very complex system of nerves. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The brain, nerves, and skeletal muscles—collectively known as the neuromuscular system—work together to cause movement. Purposeless and uncoordinated movements can be extremely disabling and may result in social isolation. Long-term degenerative disorders of the neuromuscular system include conditions in which neurologic function deteriorates over time. Such disorders are usually unpreventable, and options for treatment are limited. This chapter discusses two disorders of the neuromuscular system: Parkinson's disease and multiple sclerosis.

11.1 Introduction to Parkinson's Disease

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 11.1.1 Describe the pathophysiology of Parkinson's disease.
- 11.1.2 Identify the clinical manifestations related to Parkinson's disease.
- 11.1.3 Identify the etiology and diagnostic studies related to Parkinson's disease.

Parkinson's disease (PD) is a progressive neurologic condition that destroys some of the dopamine-secreting neurons of the substantia nigra, a critical area of the brain that produces dopamine and has an important role in controlling an individual's movements. Dopamine loss occurs in other regions of the brain as well, including the

brainstem, thalamus, and cortex. Noradrenergic neurons require dopamine in order to produce norepinephrine, and in PD, these neurons are also adversely affected. Both dopamine and norepinephrine are necessary catecholamines to keep the body regulated during the stress response. The substantia nigra is one of the structures of the basal ganglia, also known as the extrapyramidal system (EPS). This area of the brain is responsible for voluntary motor movement, posture, and cognitive and emotional functions. Several neurotransmitters mediate communication in this region, including glutamate (excitatory), dopamine (generally excitatory), gamma-aminobutyric acid (GABA; inhibitory), and acetylcholine (ACh) (excitatory or inhibitory).

The condition occurs predominantly in middle-aged and older adults. This disease affects approximately 1 million people in the United States. Furthermore, it is estimated that 90,000 new cases are diagnosed each year. The average life expectancy of a person with PD is generally the same as for people who do not have the disease (Parkinson's Foundation, 2023b). The progression of clinical manifestation varies slightly for each individual because the disease is highly diverse (Parkinson's Foundation, 2023e).

SPECIAL CONSIDERATIONS

Gender and Geographic Differences in the Incidence of Parkinson's Disease

- PD affects males 1.5 times more often than females.
- Incidence is higher in certain geographic regions: the "Rust Belt" (parts of the northwestern and midwestern United States previously regulated by industrial manufacturing), Southern California, Southeastern Texas, Central Pennsylvania, and Florida.

(Source: Parkinson's Foundation, 2023d)

Etiology

The exact cause of PD is still unknown. Theories exist related to the causes of the degeneration of the basal ganglia including viral infections, blunt head trauma, encephalitis, atherosclerosis, and exposure to certain drugs and environmental factors, such as pesticides. There is also most likely an interaction between genetic predisposition and environmental factors. Parkinson-like symptoms may arise because of antipsychotic drugs. Antipsychotics block dopamine receptors, interfering with the same neural pathway and functions affected by the insufficient amount of dopamine. They also produce movement disorders, which involve extrapyramidal reactions, such as **dystonia** (involuntary muscle contractions causing repetitive or twisting movements), **akathisia** (restless, constant moving), **tardive dyskinesia** (sudden involuntary and uncontrollable movements), and parkinsonism (stooped posture, shuffling gait, and muscle rigidity). Antipsychotics are discussed in more detail in Psychopharmacologic Drugs.

Pathophysiology

A part of the basal ganglia called the substantia nigra (see Figure 11.2) contains nerves that secrete dopamine; this secretion of dopamine progressively degenerates with PD. Because the basal ganglia works with the cerebral cortex and thalamus, it helps with both coordination of complex patterns of motor activity and cognitive control of motor activity. In PD, neurons in the substantia nigra begin to **atrophy**, become impaired, or die; some contain Lewy bodies, which are **alpha-synuclein** protein aggregates that impair transport of dopamine and contribute to neuronal death. Mutations in the mitochondria, resulting in free radicals, can also damage membranes, proteins, DNA, and other components of the cells in PD. Furthermore, depigmentation of the dopamine-producing neurons contributes to an inflammatory response from the extracellular melanin (pigments produced by melanocytes that gives color to the skin and eyes) in surrounding brain tissue (Capriotti, 2020). Another midbrain structure, called the ventral tegmental area (VTA), also contains cell bodies that produce dopamine essential for movement. The VTA is also involved in PD and gradually degenerates as the disease progresses.

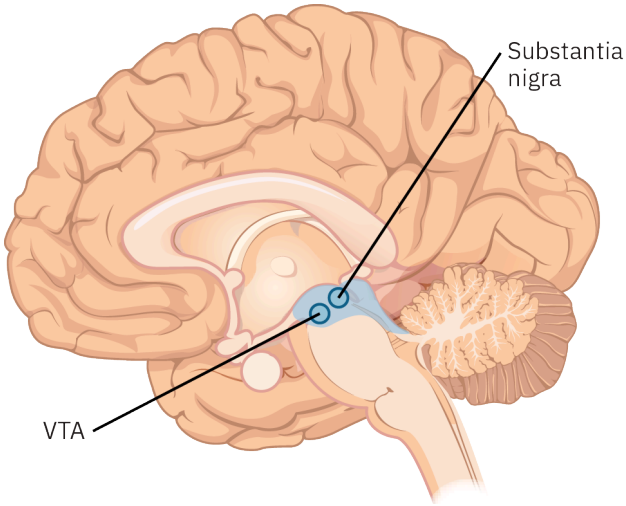


FIGURE 11.2 The substantia nigra is part of the basal ganglia. It contains nerves that secrete dopamine; the amount of dopamine secreted decreases with PD. (credit: modification of work from *Psychology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The two major neurotransmitters implicated in the disease process are dopamine and acetylcholine (ACh). The correct ratio of these neurotransmitters is essential in regulating balance, posture, standing, walking, and writing. People with PD have an imbalance that results in a decrease in dopamine and an excess of ACh. With the lack of dopamine, the excitatory ACh is the dominant neurotransmitter. There are also multiple glutamate pathways that are excitatory in this area of the brain. The result of this imbalance between excitation and inhibition of the motor system is apparent as the manifestations of PD arise (Capriotti, 2020).

Diagnostics

Currently, no single definitive test exists to diagnose PD. The diagnosis is based on these factors:

- Medical history and clinical manifestations
- Blood and laboratory tests to rule out other disorders that may be causing the symptoms
- Brain scans to rule out other disorders (Note that computed tomography [CT] and magnetic resonance imaging [MRI] scans of people with PD usually appear unremarkable.)
- Positron emission tomography (PET) or single photon emission CT (SPECT) that show reduced uptake of dopaminergic markers
- Substantial and sustained responses to medications for PD

In rare cases, where people have a clearly inherited form of PD, researchers can test for known gene mutations as a way of determining an individual's risk of developing the disease (Capriotti, 2020; Mayo Clinic, 2023).

Clinical Manifestations

Motor symptoms of PD occur late in the disease process. Usually 60%–80% of the dopamine-releasing neurons of the substantia nigra are already destroyed before the onset of motor symptoms (Parkinson's Foundation, 2023e).

The four primary motor manifestations of overt PD (shown in Figure 11.3) are (Capriotti, 2020; National Institute of Neurological Disorders and Stroke, 2023b):

- *Tremors:* This involuntary quivering is progressive and often begins in one isolated area, such as the head or hands, and then often spreads to the legs. Tremors are seen when the body is at rest and disappear upon purposeful movement or during sleep. "Pill rolling" is a classic behavior. Clients rub the thumb and forefinger together as if an actual pill were between them. The tremors usually begin unilaterally but become bilateral as time progresses.
- *Rigidity:* **Rigidity** involves stiffness—the resistance to movement by both flexors and extensors. During passive range of motion, there is resistance and the client exhibits jerky movements, also known as cogwheel rigidity. The tongue and throat may become involved, leading to difficulty swallowing and talking. The client's speech becomes soft and monotone with difficulty articulating words.

- *Bradykinesia:* This slowed movement is the most noticeable of all the symptoms. Clients with PD have difficulties initiating movement, such as walking or getting up out of a chair. Additionally, they have difficulty controlling fine muscle movements due to the loss of dexterity. Their writing becomes small and cramped, which is referred to as **micrographia**. During ambulation, clients can be seen shuffling their feet and not taking normal strides. **Bradykinesia** may progress to akinesia, which is the inability to move. Also, clients usually present with an expressionless face or flat affect due to facial rigidity. Blinking of the eyes is minimal. This is referred to as "masked face."
- *Postural instability:* Clients with PD often demonstrate a stooped posture. They have a reduced arm swing and take small, quick steps while walking. They also may stop suddenly while walking. They do not have postural reflexes, so making corrective adjustments is challenging. The result is impaired balance and increased risk of falls. This symptom usually occurs later in the disease progression.

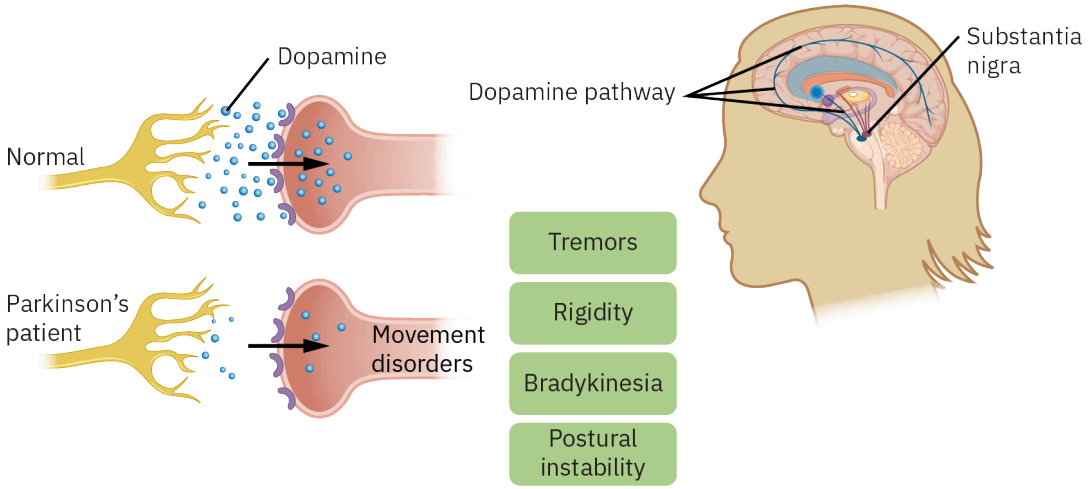


FIGURE 11.3 The lack of dopamine results in abnormal motor movements called dyskinesias. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Clients with PD also lose nerve endings that usually produce norepinephrine (NE). The neurotransmitter, NE, is the main chemical messenger that controls many automatic bodily functions. The loss of NE may explain several nonmotor manifestations seen in PD, including:

- Mood changes, such as depression and anxiety
- Cognitive changes, such as memory loss, impaired judgment, poor decision-making, and dementia
- Perceptual disturbances, such as hallucinations, delusions, and psychosis
- Sexual dysfunction due to the effects on nerve signals from the brain
- Sleep dysfunction (difficulty staying asleep, nightmares, acting out dreams that can be harmful)
- Difficulty with chewing and swallowing
  - Food and saliva may collect in the mouth and back of the throat, which can result in choking or drooling. It may be difficult for the client to obtain adequate nutrition.
- Autonomic symptoms, such as orthostatic hypotension, inability to release body heat, constipation, blurred vision, oily skin on the face, daytime sleepiness, and nighttime insomnia

Pharmacologic Management

Pharmacotherapy is essentially given to reduce distressing symptoms experienced in clients who have PD. The overall goal of medication is to maximize independence and mobility. With PD, there is too little dopamine and too much ACh, so the approach to treatment is to restore the balance between the two neurotransmitters. Drugs are classified into two broad categories: (1) dopamine agonists that directly or indirectly activate dopamine receptors through multiple mechanisms and (2) anticholinergic agents that block ACh receptors (National Institute of Neurological Disorders and Stroke, 2023b).

Nonpharmacologic Management

Nonpharmacologic strategies to slow the decline of motor function and/or manage the clinical manifestations of PD

include physical therapy to encourage clients to be as active as possible and prevent skeletal deformities, occupational therapy to teach clients how to use adapted tools and methods to make activities of daily living easier, and speech therapy to help clients swallow safely and possibly assist with speech dysfunctions. Exercise is essential to increase strength, flexibility, and balance along with reducing depression and/or anxiety. Some alternative therapies that also may improve muscle strength and flexibility and reduce risk of falls are yoga and tai chi. To enhance mental well-being and reduce pain, meditation or relaxation techniques are useful (Mayo Clinic, 2023). Deep brain stimulation has been found to be effective in reducing tremors, bradykinesia, and rigidity. A pulse generator sends controlled electrical signals to electrodes surgically implanted in the brain. The electrodes painlessly stimulate the brain to block signals that cause many of the motor symptoms (Mayo Clinic, 2023).

LINK TO LEARNING

Living with Parkinson's Disease: Michael J. Fox

Access multimedia content (https://openstax.org/books/pharmacology/pages/11-1-introduction-to-parkinsons-disease)

On *CBS Sunday Morning,* Michael J. Fox, who was diagnosed with PD at age 29, shared his story of how he reacted when first diagnosed. "Michael J. Fox on his Fight Against Parkinson's" is a 10-minute testimonial about living with PD. Fox was very open about his feelings and spoke positively about the future.

11.2 Anti-Parkinsonian Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 11.2.1 Identify the characteristics of drugs used to treat Parkinson's disease.
- 11.2.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of drugs used to treat Parkinson's disease.
- 11.2.3 Describe nursing implications of drugs used to treat Parkinson's disease.
- 11.2.4 Explain the client education related to drugs used to treat Parkinson's disease.

Currently there is no cure for PD. Although pharmacologic management is a first-line treatment, drugs only provide symptomatic relief; they do not cease or reverse the neuronal degeneration. Unfortunately, although symptoms may significantly improve at first, the symptoms frequently reappear over time as the disease worsens and drugs become less effective.

Drugs are given to restore the balance of dopamine and ACh in certain areas of the brain. This can be achieved by increasing dopamine levels with dopaminergics (classes of drugs that have different mechanisms of action), such as dopamine agonists, monoamine oxidase-B (MAO-B) inhibitors, and catechol-*O*-methyltransferase (COMT) inhibitors. Drugs are also given to block the excitatory actions of ACh. These are cholinergic antagonists (anticholinergics). Many times, the client is on combination therapy to prolong the therapeutic effects. Notably, administering exogenous dopamine is not an option because it has difficulty crossing the blood–brain barrier and has an extremely short half-life.

Anticholinergics

Anticholinergics are not as frequently used as they were in the past due to their multiple adverse effects. Several interchangeable terms are used for the medication class of anticholinergics—cholinergic blockers, muscarinic antagonists, and parasympatholytics—all of which have the same meaning. Anticholinergic agents produce their effects by preventing the activation of muscarinic receptors. These drugs work in opposition to cholinergic agonists. The two most common anticholinergics are benztropine mesylate and trihexyphenidyl hydrochloride (Parkinson's Foundation, 2023a).

CLINICAL TIP

Differences in Receptor Sensitivity

Not all muscarinic receptors are equally sensitive to blockade by most of the anticholinergic agents. At some sites, only a small concentration of drug is required to effectively block receptors. These drugs are considered high-potency agents. At other sites, a higher concentration is needed. Using higher concentrations of a muscarinic antagonist will result in increased risk of adverse effects.

Benztropine mesylate possesses both anticholinergic and antihistaminic effects, although only the anticholinergic action has been established to be the source of therapeutic effectiveness in managing PD. Despite the ability to divide doses into two or three daily, clients experience greatest relief by taking the entire dose at bedtime. The drug's long duration of action makes it suitable for bedtime medication because its effects may last throughout the night, enabling clients to turn in bed during the night more easily and to rise in the morning without having much difficulty (DailyMed, *Benztropine Mesylate,* 2021).

There are no significant differences between trihexyphenidyl and benztropine. Both are predominantly used for reducing tremors and dystonia in younger people. The drugs should be avoided in the older adult client due to the potential adverse effects.

Table 11.1 lists common anticholinergics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Benztropine mesylate (Cogentin)	*Tablets (EPS except tardive dyskinesia):* 1–4 mg orally once or twice daily. In some clients, this will be adequate; others may require more or less. *Intravenously (acute dystonic reaction):* 1–2 mg daily, followed by 1–2 mg orally twice daily to prevent recurrence.
Trihexyphenidyl hydrochloride (Artane)	*Tablets:* Initial dose: 1 mg orally the first day; can be increased by 2 mg increments every 3–5 days until a total of 6–10 mg is given daily. Total daily dose will depend on what is found to be the optimal level. Many clients derive maximum benefit from 6–10 mg daily.

TABLE 11.1 **Drug Emphasis Table: Anticholinergics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

This drug classification can cause numerous adverse effects, which is why it is not used as commonly as it was in the past. Anhidrosis can occur from the decreased secretion from sweat glands. This can be dangerous because the body is unable to release heat, which can lead to hyperthermia or heat stroke. Dry mouth, due to the decrease in salivation, can become very severe, resulting in difficulty with swallowing or speaking. This increases the client's risk for choking and/or aspiration pneumonia. Dry mouth can also cause dental caries, halitosis (bad breath), gum problems, and oral infections. A slight reduction in dosage may control nausea and still give sufficient relief of symptoms (DailyMed, *Benztropine Mesylate,* 2021; Parkinson's Foundation, 2023a).

Clients with mental disorders may experience an intensification of mental symptoms. In such cases, anti-Parkinsonian drugs can precipitate a toxic psychosis characterized by confusion, memory impairment, visual hallucinations, delusions, and nervousness. Clients with mental disorders should be kept under careful observation.

Blockade of cholinergic receptors in the eye may precipitate or aggravate glaucoma because it increases the aqueous humor in the anterior chamber by disrupting the exit of the fluid. In addition, these drugs cause mydriasis (pupil dilation) by blocking muscarinic receptors on the ciliary muscle and sphincter of the iris; paralysis of the iris sphincter results, preventing pupil constriction. The eye is unable to adapt to bright light, which causes photophobia, or intolerance to light (DailyMed, *Benztropine Mesylate*, 2021; Parkinson's Foundation, 2023a).

Blocking cardiac muscarinic receptors will eliminate parasympathetic nervous system influence on the heart. Anticholinergics cause an increase in heart rate, which can cause dysrhythmias in a client with preexisting tachycardia or a co-existing condition, such as hyperthyroidism. Urinary retention can occur due to the blockade of muscarinic receptors of the urinary tract. This relaxes the detrusor muscle, which reduces pressure within the bladder and increases the tone of the urinary internal sphincter, placing the client at risk for urinary tract infections.

Also, muscarinic antagonists block receptors in the intestine, decreasing the tone and motility of the intestinal smooth muscle. This can result in constipation or paralytic ileus. Furthermore, because anticholinergics block muscarinic receptors in the bronchi, they can promote bronchial dilation. This is a benefit for those who have asthma; however, these drugs also cause drying and thickening of bronchial secretions, which can lead to mucus plugging. Clients with asthma must be closely monitored (Capriotti, 2020).

If a client has any type of intestinal or urinary obstruction, like benign prostatic hypertrophy, these medications should be avoided because they will worsen the condition. Those with a diagnosis of myasthenia gravis should avoid anticholinergics because they could further reduce ACh's ability to send signals, which could worsen symptoms or trigger a crisis.

Antihistamines, first-generation antipsychotics, and tricyclic antidepressants should not be used concurrently with anticholinergics because these agents also possess antimuscarinic properties. The combination of multiple anticholinergic drugs can worsen the adverse effects mentioned previously. The use of alcohol can increase the risk of psychosis. Cholinergic agents, such as bethanechol used for urinary retention, can negate the effects of the anticholinergic agents because these drugs stimulate the parasympathetic nervous system by mimicking the action of ACh.

Table 11.2 is a drug prototype table for anticholinergics featuring benztropine mesylate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Centrally acting cholinergic blocker (anticholinergic) **Mechanism of Action** Exerts a direct inhibitory effect upon the parasympathetic nervous system by blocking muscarinic receptors in the striatum, thus preventing receptor stimulation from endogenous ACh or drugs that act as muscarinic agonists	**Drug Dosage** *Tablets (EPS except tardive dyskinesia):* 1–4 mg orally once or twice daily. In some clients, this will be adequate; others may require more or less. *Intravenously (acute dystonic reaction):* 1–2 mg daily, followed by 1–2 mg orally twice daily to prevent recurrence.
Indications As adjunct therapy for all forms of parkinsonism For control of extrapyramidal disorders (except tardive dyskinesia) caused by neuroleptic drugs **Therapeutic Effects** Improves the balance between dopamine and ACh levels Can reduce resting tremors, along with possible rigidity and bradycardia	**Drug Interactions** Antihistamines First-generation antipsychotics Tricyclic antidepressants Cholinergic agonists (parasympathomimetics) **Food Interactions** Alcohol
Adverse Effects Confusion/agitation **Anhidrosis** Dry mouth (xerostomia) Hyperthermia/heat stroke Tachycardia Urinary retention Constipation/paralytic ileus Bronchial plugging Nausea/vomiting Psychosis/visual hallucinations/tardive dyskinesia Blurred vision/dilated pupils/photophobia Increases intraocular pressure Muscarinic antagonist poisoning	**Contraindications** Children ≤3 years of age Hypersensitivity to ingredients of drug Caution: Children >3 years of age Tachycardia Individuals who work outside in hot weather Central nervous system (CNS) disease Angle-closure glaucoma Benign prostatic hypertrophy (BPH) Intestinal or urinary obstruction Tardive dyskinesia Myasthenia gravis

TABLE 11.2 **Drug Prototype Table: Benztropine Mesylate** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

American Geriatrics Society Beers Criteria ®

Anticholinergic drugs are designated as potentially inappropriate for use in adults 65 years and older because older adults are very sensitive to the adverse effects like orthostatic hypotension, urinary retention, constipation, and tachycardia. Sedation, confusion, and blurred vision are risk factors for falls.

(Source: American Geriatrics Society, 2023)

Nursing Implications

The nurse should do the following for clients who are taking anticholinergics:

- Assess for decreased rigidity and tremor.
- Monitor client's ability to engage in self-care tasks and walk independently.
- Assess for an increase in heart rate and/or blood pressure.
- Monitor for any signs of respiratory distress or moist, nonproductive cough.
- Assess level of consciousness and orientation.
- Darken room for photophobia due to mydriasis (dilated pupils).

- Ensure the client is receiving proper oral hygiene.
- Encourage frequent sips of water to prevent dehydration.
- Assess for difficulty with swallowing—if needed, request consult with occupational therapy.
- Assess for speech impairments—if needed, request consult for speech pathologist.
- Monitor intake and output for reduction of urine output and positive net balance.
- Perform a bladder scan to assess for residual volume of urine due to urinary retention.
- Assess for signs and symptoms of paralytic ileus, such as constipation, abdominal pain, diminished bowel sounds, and abdominal distention.
- Assess for muscle weakness.
- Provide frequent rest periods during the day to avoid aggravating the tremors and rigidity.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an anticholinergic should:

- Have an understanding that PD is not curable, but treatment can significantly reduce symptoms.
- Be advised to report gastrointestinal complaints, fever, or heat intolerance promptly.
- Minimize urinary retention by voiding just before taking the medication.
- Keep lighting dim to avoid discomfort due to pupillary dilation. Wear dark glasses when out in the sun.
- Engage in physical therapy to increase balance and strength.
- Wear shoes that slip on and clothing that contains Velcro or zippers for easier handling.
- Avoid alcohol and sedatives, including over-the-counter medications that contain these.
- Drink water frequently.
- Keep sugarless hard candy or gum on hand to minimize the dry mouth.
- Maintain adequate dental/oral hygiene.
- Visit the ophthalmologist and dentist regularly.
- Consume adequate dietary fiber and fluid.

The client taking an anticholinergic *should not:*

- Engage in strenuous activity outside when the temperature is high.
- Drive or perform hazardous tasks if their vision or alertness is impaired.
- Rise or change positions quickly due to possible orthostatic hypotension.
- Stop drugs abruptly because symptoms will quickly reoccur.
- Overexert themselves; they should take rest periods between activities.

Dopaminergics

Dopaminergic means related to dopamine. Dopamine constitutes approximately 80% of the **catecholamine** content within the brain. Dopamine is known to have an essential role in nearly all cognitive functions, including self-initiated motor control, motivation, and learning (Costa & Schoenbaum, 2022). Dopaminergic substances increase dopamine-related activity in the brain. These dopaminergic substances are also referred to as dopamine replacers when dopaminergic neurons are dysfunctional or destroyed, such as what occurs in PD. Neurons that synthesize or contain dopamine and synapses with dopamine receptors in them may also be labeled as dopaminergic. Enzymes that regulate the biosynthesis or metabolism of dopamine, such as dopamine decarboxylase, MAO, and COMT, also are deemed dopaminergic. In addition, any endogenous or exogenous chemical substances that affect dopamine receptors or dopamine release can be said to have dopaminergic properties. Two prominent examples are opioids and amphetamines.

Levodopa

Levodopa was introduced in the 1960s and has been a cornerstone of PD treatment for many years (Ovallath & Sulthana, 2017). Levodopa is a metabolic precursor of dopamine and is inactive until it undergoes conversion to its active state. This drug has proven to be extremely beneficial in the early stages of PD. Unfortunately, over time, the

number of neurons decreases, and fewer cells are capable of converting the levodopa to dopamine. Motor fluctuations then develop, and the client experiences the relief of symptoms only when the drug is present.

The purpose of this drug is to replenish the brain's reduced supply of dopamine by increasing dopamine synthesis. Levodopa is absorbed in the blood from the small intestine and travels through the circulation to the brain. Once it crosses the blood–brain barrier, it binds to dopamine receptors on GABA neurons, helping to restore the balance between neurotransmitters (Parkinson's Foundation, 2023b).

Levodopa is not used as a monotherapy; given alone, it is not beneficial. It should be administered with carbidopa (discussed later in this chapter). Without the combination, a large majority of levodopa gets decarboxylated in the periphery—causing systemic effects such as nausea and vomiting, dysrhythmias, and hypotension—and resulting in less levodopa crossing the blood–brain barrier. The drug combination increases the amount available to cross the blood–brain barrier.

Inbrija is an inhaled levodopa powder that is a dopamine precursor commonly used for early morning or sudden "off" episodes. These episodes are seen when levodopa's effects wear off before the next dose is due. The inhalation route enables a low but quicker acting boost of dopamine. Inbrija is not intended to replace a client's maintenance medications but is given concurrently with levodopa/carbidopa. The drug comes in a capsule and must be administered through the appropriate inhaler device. Inhalation-specific contraindications include asthma, chronic obstructive pulmonary disease, or other long-term underlying lung disease (DailyMed, *Inbrija*, 2023).

Carbidopa/Levodopa

Carbidopa is a dopamine decarboxylase inhibitor; combined with levodopa, levodopa's effects are enhanced. The drug inhibits decarboxylation of levodopa in the intestines and peripheral tissues. Therefore, less levodopa is converted into dopamine within the periphery, and more is available to cross the blood–brain barrier. This is beneficial, not only to increase the amount of dopamine that reaches the brain, but also to diminish the adverse effects dopamine causes when circulating in the periphery. Combining levodopa with carbidopa allows the dosage of levodopa to be reduced by 75%. Carbidopa has no pharmacological effects on its own and is unable to cross the blood–brain barrier. This drug combination stops the motor symptoms early in the disease process but has no effect on the disease itself.

Therapeutic effects may not be seen for weeks or months. This drug should be taken on an empty stomach, typically 30 minutes before a meal. Food can significantly decrease absorption, especially a large amount of protein. Carbidopa decreases nausea and vomiting and the cardiovascular response by reducing the amount of dopamine in the periphery (DailyMed, *Sinemet,* 2022). Levodopa comes in multiple forms and is administered via several routes, including oral (immediate-release, control-release, and extended-release) tablets, intestinal gel, and inhalation.

DUOPA is the intestinal gel form of carbidopa/levidopa delivered through a surgically implanted tube in the small intestine. This drug is used for clients who have advanced disease and have difficulty swallowing. The overall goal of this delivery method is to increase "on" time episodes. The maximum recommended daily dose of DUOPA is 2000 mg administered over 16 hours (Parkinson's Foundation, 2023b). Distinct contraindications for this route include complications from the insertion of the intestinal tube or incision site inflammation (DailyMed, *DUOPA*, 2022).

Table 11.3 lists common dopaminergics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Levodopa (Inbrija)	*Inhaled:* 84 mg capsule up to 5 times daily as needed.
Carbidopa/levodopa immediate-release tablet (Sinemet) Carbidopa/levodopa oral disintegrating tablet (Parcopa)	*Immediate-release tablet:* Initial dose: 1 25–100 mg tablet 3 times daily. Dosage may be increased by 1 tablet every day or every other day, as necessary, up to 8 25–100 mg tablets daily. *Oral disintegrating tablet (ODT):* Levodopa must be discontinued at least 12 hours before starting ODTs. A daily dosage should be chosen that will provide approximately 25% of the previous levodopa dosage. Clients taking <1500 mg of levodopa daily should be started on one 25 mg/100 mg tablet 3–4 times daily. Clients taking ≥1500 mg should start on 1 25 mg/250 mg tablet 3–4 times daily. At least 70–100 mg of carbidopa daily should be provided for both types of tablets.
Carbidopa/levodopa extended release (Rytary)	Levodopa must be discontinued at least 12 hours before this therapy. *Mild to moderate disease:* Initial dose: 1 50 mg/200 mg tablet twice daily. Maintenance dose: 400–1600 mg daily administered in divided doses every 4–8 hours.

TABLE 11.3 **Drug Emphasis Table: Dopaminergics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Nausea and vomiting are common symptoms that usually disappear after a few months on levodopa/carbidopa. The symptoms are usually caused by activation of dopamine receptors in the chemoreceptor trigger zone, which contains receptors that detect emetic agents in the blood and relay that information to the vomiting center. This is reduced with carbidopa. Carbidopa can be given as a single drug (Lodosyn). If added to levodopa/carbidopa, the extra carbidopa can reduce levodopa-induced nausea and vomiting. It also allows smaller doses of levodopa to be used while promoting a faster response.

Conversion of levodopa to dopamine in the periphery can produce excessive activation of beta-adrenergic receptors in the heart. Dysrhythmias can result, especially in clients with heart disease. Clients with preexisting coronary artery disease may take propranolol to counteract cardiac dysrhythmias.

"Wearing off" develops near the end of the dosing interval, indicating drug levels have declined to a subtherapeutic value. This can be minimized in three ways: (1) shortening the dosing interval, (2) giving a drug that prolongs levodopa's plasma half-life (MAO-B inhibitors or COMT inhibitors), or (3) giving a direct-acting dopamine agonist. "On-off" episodes occur any time during the dosing interval, even if drug levels are high. These episodes may last from minutes to hours. Over time, off periods usually increase in both intensity and frequency. One reason these episodes occur in PD is because the gastrointestinal (GI) motility decreases, delaying absorption of levodopa and altering serum levels.

About 80% of clients treated with levodopa will experience drug-induced **dyskinesias** during the advanced stages of the disease, and 30% will develop it after only 3 years of levodopa treatment (Kwon et al., 2022). Some of these are just bothersome (head bobbing tics, grimacing), whereas others can be disabling, such as **ballismus**—rapid, involuntary jerking or flinging of proximal muscle groups—or **choreoathetosis**—slow, involuntary, writhing movements. Levodopa exacerbates symptoms of psychosis, possibly through the buildup of central dopamine. Urine and sweat can become brownish because of the melanin produced from catecholamine oxidation.

This drug can cause clients to become impulsive. Clients may either begin to engage in or increase already existing gambling/sexual urges or uncontrolled spending. This is due to the increase of dopamine in the brain.

There have been reports of clients suddenly falling asleep without warning of feeling drowsy. Before these sleep attacks, the clients were engaged in performing activities of daily living, driving a vehicle, or conversing. If these occur, the drug should be discontinued. Importantly, the drug should not be stopped abruptly because it could lead

to the reemergence of signs and symptoms of PD, sometimes worse than the initial manifestations. It could also lead to confusion, muscle rigidity, autonomic instability, and hyperpyrexia, which resembles **neuroleptic malignant syndrome (NMS)**.

Narrow-angle glaucoma is a contraindication as levodopa can worsen the condition due to the potential of further increase of intraocular pressure.

Epidemiological studies have shown that clients with PD have a higher risk (two- to approximately six-fold) of developing melanoma than the general population. It is unknown whether this is due to PD itself or the drugs used in the treatment of PD. Clients and providers are advised to monitor for melanomas frequently and on a regular basis when using carbidopa and levodopa for any indication. Ideally, periodic skin examinations should be performed by appropriately qualified individuals (e.g., dermatologists).

First-generation antipsychotics block receptors for dopamine in the striatum, diminishing the therapeutic effects of levodopa. This may augment Parkinsonian symptoms. Low doses of atypical antipsychotics are sometimes used to treat levodopa-induced psychotic symptoms. Nonselective monoamine oxidase inhibitors (MAOIs) can result in a hypertensive crisis if administered to a client taking levodopa. Nonselective MAOIs should be withdrawn at least 2 weeks before starting levodopa. Dopamine receptor antagonists, such as phenothiazines, risperidone, or metoclopramide, should be avoided because they will decrease the effects due to their dopamine receptor antagonistic properties.

If levodopa is administered alone, pyridoxine (B_6) will decrease its effects (greater than 200 mg daily) because it enhances decarboxylase and increases peripheral breakdown of levodopa. If given in combination with carbide, this is not a concern. Other antihypertensives can exacerbate orthostatic hypotension. Iron salts can form chelates with levodopa and reduce its bioavailability. Because amino acids compete with levodopa for intestinal absorption and for transport across the blood–brain barrier, high-protein foods will reduce levodopa's therapeutic effects.

Table 11.4 is a drug prototype table of dopaminergics featuring oral carbidopa/levodopa. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Dopaminergic **Mechanism of Action** Taken up by dopaminergic nerve terminals in the striatum, where it is converted into dopamine and then released into the synaptic space and binds to dopamine receptors	**Drug Dosage** Levodopa must be discontinued at least 12 hours before this therapy. *Mild to moderate disease:* Initial dose: 1 50 mg/200 mg tablet twice daily. Maintenance dose: 400–1600 mg daily administered as divided doses every 4–8 hours.
Indications Reduces symptoms of PD by increasing dopamine synthesis **Therapeutic Effects** Decreases rigidity, tremors, and other symptoms of nonmotor symptoms	**Drug Interactions** Nonselective MAOIs Antipsychotics (first generation) Pyridoxine (B_6) decreases effects (>200 mg daily) Antihypertensives Iron salts Dopamine receptor antagonists **Food Interactions** High protein
Adverse Effects Wearing-off phenomenon (gradual) On-off phenomenon (abrupt) Nausea and vomiting Dose-related dyskinesias (abnormal movements) Orthostatic hypotension Tachycardia/dysrhythmias/chest discomfort Psychosis (visual and auditory hallucinations, nightmares, paranoia, dementia) Brownish urine and sweat Depression/anxiety/suicidal ideations Impulse control Sleep attacks Cough/expectoration of sputum, headache, and reduced red blood cell count (inhaled form)	**Contraindications** Known hypersensitivity to any component of drug Narrow-angle glaucoma

TABLE 11.4 **Drug Prototype Table: Carbidopa/Levodopa** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Similarly Named Drugs

Do not confuse Sinemet (dopaminergic) with Janumet (antidiabetic).

(Source: ISMP, 2023)

CLINICAL TIP

Combination Drug (Stalevo)

Stalevo is a combination of levodopa, carbidopa, and entacapone. This fixed-dose combination drug enhances the amount of levodopa that reaches the brain. Both carbidopa and entacapone prevent the breakdown of levodopa within the periphery, decreasing the dopamine effects in the periphery. In addition, this drug can significantly reduce the "wearing off" time experienced by levodopa. The combination form increases adherence because the client only needs to take one drug versus two different ones. For more information about this combination drug, please refer to each individual agent discussed above (DailyMed, *Stalevo*, 2021).

Nursing Implications

The nurse should do the following for clients who are taking dopaminergics:

- Encourage slow position changes to minimize postural hypotension.
- Assess neurological status, such as orientation, grip strength, gait, reflexes, tremors, or spasticity.
- Inform client that hallucinations and other psychotic behavior can occur, and these will be treated appropriately.
- Evaluate therapeutic effects—decrease in drooling, tremors, bradykinesia, or rigidity and increase in facial expressions.
- Space activities evenly throughout the day for adequate rest periods.
- Monitor serum liver enzymes, hemoglobin/hematocrit, bilirubin, blood urea nitrogen (BUN), Coombs tests, and elevated serum glucose periodically throughout treatment.
- Monitor for involuntary movements of the tongue, mouth, and face.
- Provide demonstration on proper technique of using the inhalation form and have client return demonstrate.
- Look for signs of increased depression or suicidal ideations.
- Specifically ask the client about feeling drowsy or sleepy while performing certain activities.
- Advise clients to exercise caution while driving, operating machinery, or working at heights.
- Ask about new or increased gambling urges, sexual urges, or uncontrolled spending.
- Monitor for melanomas frequently by performing a thorough skin assessment.
- Explain to client that the color of the urine may become brownish orange, but this is harmless.
- Provide dietary counseling about high-protein foods and to evenly space their intake throughout the day.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a dopaminergic should:

- Have an understanding that they will not experience immediate improvement. Therapeutic responses will steadily increase over the first few months.
- Take their medications even if not experiencing symptoms.
- Sit or lie down if dizziness occurs and wait until it subsides before standing or walking.
- Space activities to obtain optimal benefit from the drug.
- Immediately notify the provider at the start of involuntary movements of the face or mouth.
- Perform a skin assessment weekly for any evidence of changes in existing lesions or an onset of lesions.
- Understand that their urine can be a brownish organ color, but this is not something to worry about.

The client taking a dopaminergic *should not:*

- Chew, break, or crush extended-release capsules.
- Swallow the capsules that are indicated for the inhalation route.
- Rise or change positions quickly due to possible orthostatic hypotension.
- Stop drugs abruptly because symptoms will quickly reoccur.
- Eat foods with high iron content, such as red meat.
- Take multivitamin preparations containing pyridoxine and/or iron salts.
- Eat a high-protein meal; they should evenly space their daily protein intake throughout the day.
- Drive or engage in activities that require alertness if experiencing sleep attacks.

Dopamine Agonists

Dopamine agonists are first-line drugs in the treatment of mild to moderate PD. These drugs mimic the role of dopamine in the brain. Their duration is longer than compared with levodopa. They are relatively selective for D2 receptors. Activating these receptors causes increased dopamine levels in the nigrostriatal pathway, which leads to smooth and coordinated movements. This classification is used as a monotherapy or in combination with levodopa. Initial therapy is associated with less risk of developing dyskinesias and motor fluctuations compared with clients

started on levodopa. Dopamine agonists may delay the need to use levodopa in early PD and may decrease the dose of levodopa in advanced PD. When used on a long-term basis, they have a lower incidence of response failures. In addition, they can be used as an adjunct medication to supplement levodopa when further dopaminergic effect is needed or if complications of levodopa treatment arise, such as dyskinesias, "wearing off," and motor fluctuations. These drugs will be ineffective in clients who do not improve with levodopa (American Parkinson Disease Association, 2014).

Dopamine agonists are divided into ergot and nonergot derivatives. The ergot derivatives are nonselective and block serotonergic and alpha-adrenergic receptors. Because of this, the ergots cause more cardiovascular concerns. The nonergot derivatives are selective for dopamine receptor subtypes. The nonergot derivatives have similar mechanisms of actions, adverse effects, and interactions. This information can be found below. Any distinct changes are mentioned with the specific drug sections.

- *Pramipexole:* A nonergot dopamine agonist that selectively binds to dopamine-2 receptor subtypes, which activates CNS postsynaptic dopamine receptors in the striatum. This drug is mainly used as a monotherapy in the early stages of PD. As the disease progresses, it is used in combination with levodopa (DailyMed, *Pramipexole dihydrochloride,* 2023).
- *Ropinirole:* Essentially the same as pramipexole. This drug should be discontinued over a 7-day period to prevent adverse reactions such as confusion, rigidity, or hyperpyrexia.
- *Rotigotine:* Similar to pramipexole, but one main difference is the route. Rotigotine is only available as a daily transdermal patch. This is beneficial for those who are unable to take oral formulations due to dysphagia. This route provides unfluctuating drug levels over 24 hours. The other difference is this drug can cause peripheral edema (cause unknown) or skin reactions at the site of application (DailyMed, *Neupro,* 2022).
- *Apomorphine hydrochloride:* Another nonergot derivative, this is a short-acting drug delivered by subcutaneous injection or sublingually. This drug is reserved as an acute "rescue" medication to treat "off" episodes in between doses or "off-on" periods that occur randomly in clients with advanced PD. Both routes have a rapid onset of action. Their mechanism of action is the same as for pramipexole. The injection route is advantageous for those unable to adequately or safely swallow. A duration of at least 2 hours between doses is highly recommended, and 5 doses a day is the maximum. To prevent a medication error, the prescribed dose needs to be written in milliliters because the multi-dose pen has markings in milliliters. This is a highly emetogenic drug (induces vomiting); therefore, it is routinely given concurrently with an antiemetic such as trimethobenzamide 300 mg three times a day starting 3 days before the first dose and continued as needed to control nausea and vomiting. Use should generally not exceed 2 months (DailyMed, *Apomorphine hydrochloride,* 2022).
- *Bromocriptine:* An ergot derivative. Because the ergot derivatives are nonselective, they block other receptors, such as serotonergic and adrenergic receptors. This causes a variety of adverse effects unseen with the nonergot derivatives (DailyMed, *Bromocriptine mesylate*, 2021).

! SAFETY ALERT

Similarly Named Drugs

Do not confuse ropinirole (dopamine agonist) with risperidone (antipsychotic).

(Source: ISMP, 2023)

Table 11.5 lists common dopamine agonists and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Pramipexole (Mirapex)	*Immediate-release tablets:* 0.125 mg 3 times daily initially; increase over 7 weeks to a maximum of 1.5 mg 3 times daily. *Extended-release tablets:* 0.375 mg daily initially; gradually increase to a maximum of 4.5 mg daily.
Bromocriptine mesylate (Parlodel)	Initial dose: 1.25 mg twice daily with meals. Doses may be increased every 14–28 days by 2.5 mg daily. Dose reduction must be done gradually in 2.5 mg increments.
Apomorphine hydrochloride (Apokyn)	2–6 mg subcutaneously for each "off" episode; maximum: 5 doses daily.
Ropinirole (Requip)	*Immediate-release tablets:* 0.25 mg 3 times daily initially; increase over several months to a maximum of 8 mg 3 times daily. *Extended-release tablets:* 2 mg daily initially; increase weekly by 2 mg over several months to a maximum of 24 mg daily.
Rotigotine (Neupro)	*Early stage:* Initial dose: 2 mg patch daily; increase by 2 mg weekly until lowest effective dose is obtained or maximum dose of 6 mg daily is reached. *Advanced stage:* Initial dose: 4 mg patch daily; increase by 2 mg weekly up to the maximum dose of 8 mg daily.

TABLE 11.5 Drug Emphasis Table: Dopamine Agonists (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Nonergot derivatives are known to produce unusual effects, such as compulsive gambling, hypersexuality, overspending, and overeating. These behaviors are dose related and will reverse when the drug is discontinued. Providers should screen for compulsive and addictive behaviors before starting medication. Also, clients may not be aware of this behavior, so they should be specifically asked about it. Another unusual effect is these medications can make one quickly fall asleep while performing daily activities. Often the person will not feel drowsy before falling asleep. This creates an elevated risk of injury and/or accidents.

Hyperhidrosis (excessive sweating unrelated to heat or exercise) is caused by the dysregulation of the autonomic nervous system, which could be related to PD or the dopamine agonist. Hyperhidrosis can result in dehydration and electrolyte loss. Older adults and clients with a history of psychiatric disorders are more sensitive and at increased risk of experiencing confusion and hallucinations. Dyskinesias are seen more frequently in the aforementioned dopamine agonists when combined with levodopa. Clinical studies have revealed this drug class has teratogenic effects and should be avoided in pregnancy and breastfeeding (DailyMed, *Pramipexole Dihydrochloride*, 2023).

Cardiovascular disease may occur due to severe hypotension and impaired perfusion. Orthostatic hypotension occurs due to a dopamine-mediated blunting of the noradrenergic response to standing and subsequent decrease in peripheral vascular resistance. Valvular heart disease occurs due to activation of serotonin receptors on the heart valves.

Antipsychotics or dopamine antagonists will cancel the dopamine agonist effects. Higher doses of estrogens reduce clearance of the drug. Starting or stopping hormone replacement therapy may require adjustment of dosage. Because significant hypotension and loss of consciousness has occurred with these drugs when taken with serotonin receptor antagonists, this combination should be avoided.

Although apomorphine is a morphine derivative, this drug does not cause analgesia, euphoria, or respiratory depression. The most common adverse reactions specific to this drug are excessive yawning, injection-site reactions, rhinorrhea, and cardiac issues. It is important to monitor cardiac status due to the associated risk for hypotension and dose-related prolongation of the QT interval. There have been reports of chest pain, myocardial infarction, dysrhythmias, and cardiac arrest. Furthermore, this drug has the potential to exacerbate coronary and cerebral ischemia in clients with known disease. Any client with an allergy to sulfites should not receive apomorphine (DailyMed, *Apomorphine Hydrochloride*, 2022).

Table 11.6 is a drug prototype table of dopamine agonists featuring pramipexole. It lists drug class, mechanism of

action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Dopamine agonist, nonergot derivative **Mechanism of Action** Selectively binds to dopamine receptor subtype that activates CNS postsynaptic dopamine receptors in the striatum; not dependent on enzymatic conversion to become active	**Drug Dosage** *Immediate-release tablets:* 0.125 mg 3 times daily initially; increase over 7 weeks to a maximum of 1.5 mg 3 times daily. *Extended-release tablets:* 0.375 mg daily initially; gradually increase to a maximum of 4.5 mg daily.
Indications Used alone in early-stage PD Combined with levodopa in advanced stages of PD **Therapeutic Effects** Monotherapy: Produces significant improvement in motor performance Combination: Reduces motor fluctuations and causes fewer dyskinesias due to lower dose of levodopa needed	**Drug Interactions** First-generation antipsychotic drugs Dopamine antagonists Serotonin receptor antagonists Hormone replacement therapy (estrogen) Drugs that can cause QT interval prolongation **Food Interactions** No significant interactions
Adverse Effects Nausea/vomiting/constipation Hallucinations Hyperhidrosis Sleep attacks/daytime sleepiness Impulse control disorders Orthostatic hypotension/bradycardia Dyskinesias	**Contraindications** None Caution: Adults >60 years of age Falling asleep during ADLs Symptomatic orthostatic hypotension Impulse control/compulsive behaviors Hallucinations and psychotic-like behavior Dyskinesia Postural deformity Renal impairment Rhabdomyolysis History of myocardial infarction/valve disease History of peripheral vascular disease

TABLE 11.6 **Drug Prototype Table: Pramipexole** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking dopamine agonists:

- Measure blood pressure and heart rate in the supine and standing positions before and after dosing.
- Emphasize to the client/caregiver to maintain safety precautions because falling asleep can suddenly occur without feeling drowsy.
- Monitor for peripheral edema and perfusion.
- Ask about compulsive and uncontrollable behaviors.
- Assess for any involuntary movements, especially with the upper and lower extremities.
- Teach client ways to cope with the excessive sweating they may experience.
- Provide clients education about high-fiber foods to reduce risk of constipation.
- Monitor routine electrocardiogram (ECG, EKG) for prolongation of QT interval when receiving apomorphine.
- Evaluate electrolytes periodically if individual has hyperhidrosis.
- Instruct client about the correct way to administer the subcutaneous apomorphine.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a dopamine agonist should:

- Be aware that they can suddenly fall asleep while performing regular daily activities.
- Sit or lie down if dizziness occurs and wait until it subsides before standing or walking.
- Notify the provider immediately if there are any signs of rashes, hives, pruritis, or facial or tongue swelling.
- Increase their intake of water if experiencing excessive sweating.
- Eat a high-fiber diet and obtain adequate exercise to reduce/prevent constipation.
- Contact the provider if experiencing involuntary movements, chest pain, and peripheral edema.
- Understand that the medication may not reach full therapeutic effect for several weeks.
- Be able to correctly demonstrate the use of the apomorphine pen delivery device and to use a new sterile needle with each injection.
- Use a different site each time they administer apomorphine.

The client taking a dopamine agonist *should not:*

- Abruptly stop the medication because this can worsen PD symptoms.
- Chew, break, or crush extended-release formulations.
- Rise or change positions quickly due to possible orthostatic hypotension.
- Take if pregnant or breastfeeding.
- Administer apomorphine intravenously due to the risk of thrombus formation or pulmonary embolism.

Monoamine Oxidase-B Inhibitors

MAO-B inhibitors block or reduce the activity of the enzyme MAO type B that breaks down dopamine in the brain. They cause dopamine to accumulate in surviving nerve cells and reduce PD symptoms. Some evidence suggests selegiline may delay neurodegeneration and disease progression. Despite no existing conclusive evidence, current guidelines suggest trying it in newly diagnosed clients because it might confer some protection (Parkinson's Foundation, 2023c).

- *Selegiline hydrochloride:* An irreversible MAO-B agent that is used with carbidopa/levodopa to enhance and prolong the response to levodopa. This may reduce the wearing-off times. Three days after starting selegiline, the health care provider can attempt to reduce the dose of levodopa to help decrease adverse effects related to levodopa. Selegiline hydrochloride causes insomnia because the drug metabolizes to methamphetamine and amphetamine, which have stimulating properties. This should improve over time (DailyMed, *Selegiline Hydrochloride*, 2023).
- *Safinamide:* A reversible MAO-B inhibitor that inhibits voltage-sensitive sodium channels and glutamate release. It is the prototype of a new generation of multi-active MAO-B inhibitors. Salfinamide originally was developed as an antiseizure agent; however, in 2017 the drug was FDA approved for the treatment of PD. This drug is used in conjunction with levodopa/carbidopa for those experiencing "off" episodes and to increase motor function and decrease motor fluctuations (DailyMed, *Xadago,* 2023).
- *Rasagiline:* The major difference between selegiline and rasagiline is that the latter drug does not convert to amphetamine and methamphetamine. Therefore, insomnia is not a concern (DailyMed, *Rasagiline Mesylate*, 2022).

Table 11.7 lists common monoamine oxidase-B inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Selegiline hydrochloride (Eldepryl)	10 mg daily, divided in 2 doses.
Safinamide (Xadago)	Initial dose: 50 mg orally daily at the same time each day. After 2 weeks, the dose may be increased to 100 mg daily dependent on individual need.
Rasagiline (Azilect)	*Monotherapy:* 1 mg once daily. *Adjunct to levodopa:* 0.5 mg once daily; increase dose to 1 mg daily as needed for sufficient clinical response.

TABLE 11.7 **Drug Emphasis Table: Monoamine Oxidase-B Inhibitors** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Similarly Named Drugs

Do not confuse selegiline (MAO-B inhibitor) with Salagen (saliva production stimulator).

(Source: ISMP, 2023)

Adverse Effects and Contraindications

Because selegiline hydrochloride causes insomnia, taking it late in the day could disrupt sleep. Severe hypertension is a possibility if administered in high doses because the drug becomes nonselective and can then inhibit both MAO-A and MAO-B. At doses less than or equal to 10 mg/day, the drug is selective for MAO-B. It does not affect MAO-A, which metabolizes tyramine, norepinephrine, epinephrine, and serotonin, unless given above the recommended dose. This subtype can cause excessive stimulation of the sympathetic nervous system (SNS), causing severe hypertension and possibly stroke. This crisis can be triggered by taking sympathomimetic drugs and by ingesting foods containing tyramine. High levels of tyramine are found in foods that are aged, cured, or fermented (DailyMed, *Selegiline Hydrochloride,* 2023).

Several opioids should not be used concurrently with this drug classification. Combining MAO-B inhibitors with morphine can increase the opioid adverse reactions. Sympathomimetics, including over-the-counter medications containing dextromethorphan, should also be avoided due to increased risk of exaggerating psychotic symptoms. Serotonin syndrome is a life-threatening condition characterized by delirium, extreme agitation, tachycardia, labile blood pressure, rigidity, and hyperthermia. Several medications, including meperidine, tramadol, and selective serotonin reuptake inhibitors (SSRIs), can increase the risk of serotonin syndrome and should be avoided. SSRIs should be stopped 2–5 weeks before the initiation of selegiline. The tapering of the SSRIs is dependent on that particular drug's half-life. Severe CNS toxicity characterized by hyperpyrexia, seizures, changes in behavioral status, agitation, muscle rigidity, and death have been reported with combining tricyclic antidepressants (TCAs) and nonselective MAOIs (DailyMed, *Selegiline Hydrochloride*, 2023).

Table 11.8 is a drug prototype table of MAO-B inhibitors featuring selegiline hydrochloride. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Selective and irreversible MAO-B inhibitor **Mechanism of Action** Selectively and irreversibly inhibits MAO-B, an enzyme that metabolizes dopamine mainly in the brain	**Drug Dosage** 10 mg daily, divided in 2 doses.
Indications Adjunctive therapy of idiopathic PD with levodopa-carbidopa in clients whose response to that therapy has decreased Helps decrease fluctuations in motor control **Therapeutic Effects** Indirectly preserves dopamine levels in the brain Enhances the effects of levodopa and substantially reduces its required dose, which is helpful in limiting the adverse effects	**Drug Interactions** Morphine Meperidine Tramadol SSRIs TCAs Sympathomimetics **Food Interactions** Foods high in tyramine if drug becomes nonselective
Adverse Effects Insomnia Headache/dizziness Depression Irritation of the buccal mucosa with orally disintegrating tablets Severe hypertension in high doses Melanoma Serotonin syndrome Impulsive control disorders Sleep attacks Dyskinesias Hallucinations/psychotic behavior QT interval prolongation	**Contraindications** Hypersensitivity to components of drug Caution: Melanoma Severe hepatic impairment Severe psychotic disorder

TABLE 11.8 **Drug Prototype Table: Selegiline Hydrochloride** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking MAO-B inhibitors:

- Perform a skin assessment to monitor for melanomas.
- Assess cardiac monitoring periodically for prolonged QT interval and episodes of angina.
- Evaluate therapeutic effectiveness of PD clinical manifestations.
- Assess mood for depression, impulsivity, and psychotic behavior.
- Monitor liver function tests routinely for elevations in liver enzymes.
- Periodically monitor clients for visual changes.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an MAO-B inhibitor should:

- Immediately notify the provider if severe headache occurs due to MAOI-induced hypertension.
- Sit or lie down if dizziness occurs and wait until it subsides before standing or walking.
- Perform a skin assessment on a routine basis and notify provider if any changes are observed.
- Establish a routine bedtime regimen to promote sleep.

- Contact the provider with any manifestations of liver damage, such as jaundice, dark urine, clay-colored stools, anorexia, or right upper quadrant pain.
- Notify health care provider of any involuntary movements.
- Routinely have an eye examination performed.

The client taking an MAO-B inhibitor *should not:*

- Exceed the recommended daily dose of 10 mg.
- Take SSRIs, TCAs, or opioids.
- Chew, break, or crush extended-release capsules.
- Stop drugs abruptly because symptoms will quickly reoccur.
- Drive or participate in activities that can be considered hazardous until the effects are known.

Catecholomethyltransferase (COMT) Inhibitors

Normally, the methylation of levodopa by COMT to 3-O-methyldopa is a minor pathway for levodopa metabolism; however, when peripheral dopamine decarboxylase is inhibited by carbidopa, the result is a significant increase of 3-O-methlydopa and the COMT pathway becomes more significant. This then competes with levodopa for entry into the CNS. The COMT inhibitors selectively and reversibly inhibit COMT. The inhibition of COMT leads to reduction of 3-O-methlydopa plasma concentrations. The outcome is more levodopa crossing the blood–brain barrier and increased levels of brain dopamine. These agents are beneficial in reducing the symptoms of the "wearing off" phenomenon seen with levodopa. The two COMT inhibitors discussed in this section differ primarily in their adverse drug reaction profiles. Entacapone is safer than tolcapone. These drugs have no direct effects on their own; they are only indicated for use with levodopa.

- *Entacapone:* A selective, reversible COMT inhibitor for the treatment of PD. When administered with levodopa and a decarboxylase inhibitor (e.g., carbidopa), increased and more sustained plasma levodopa concentrations are reached as compared with the administration of levodopa and carbidopa given alone. It is believed that at a given frequency of levodopa administration, these more sustained plasma levels of levodopa result in more constant dopaminergic stimulation in the brain, leading to a greater reduction in the manifestations of Parkinsonian syndrome PD (DailyMed, *Entacapone*, 2022).
- *Tolcapone:* Tolcapone should be reserved for clients who cannot be treated adequately with safer drugs. This drug can cause severe, sometimes fatal, hepatocellular injury. Before treatment, clients must be fully informed of the risks and then sign an acknowledgment consent form confirming their understanding. Liver monitoring is a requirement at baseline and periodically throughout therapy. If there is any evidence of liver damage, tolcapone should be discontinued and not be used again. The enzymes generally decline within several weeks once the drug is stopped (DailyMed, *Tasmar*, 2020).

Table 11.9 lists common COMT inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Entacapone (Comtan)	Initial dose: 200 mg taken with the levodopa/carbidopa dose; can increase to a maximum of 8 doses (1600 mg daily).
Tolcapone (Tasmar)	Initial dose: 100 mg 3 times daily; increase to 200 mg 3 times daily if necessary. The first dose should be administered in the morning along with levodopa/carbidopa. The next 2 doses are taken 6 and 12 hours later.

TABLE 11.9 **Drug Emphasis Table: COMT Inhibitors** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Most of the adverse effects of these drugs result from the increased dopamine levels. These can be managed by decreasing the levodopa dose. GI and urinary adverse reactions are the most common manifestations of the COMT inhibitors themselves. Notably, only 10% of the dose is excreted in the urine; the remaining 90% is through biliary excretion. If there is biliary obstruction, these drugs may not get eliminated adequately and will accumulate.

There are reports of clients suddenly falling asleep without warning of feeling drowsy. If this occurs, the COMT inhibitors should be discontinued because these sleep attacks can recur.

Because these drugs increase dopamine (pleasure neurotransmitter) in the brain, they can cause intense urges to gamble, engage in sex, or spend money uncontrollably. In these cases, it may be necessary to reduce the dose or stop it altogether. Diarrhea can be experienced and is thought to be caused by drug-induced microscopic colitis. Diarrhea can lead to associated weight loss, dehydration, and electrolyte imbalance. If this occurs, the drug should be discontinued.

Dyskinesia occurs because entacapone potentiates the dopaminergic side effect of levodopa and may either cause or worsen preexisting dyskinesia.

Entacapone can increase levels of methyldopa, dobutamine, and isoproterenol because they are metabolized by the COMT enzyme. The accumulation of these drugs results in tachycardia, elevated blood pressure, and possible arrhythmias. Nonselective MAOIs should not be used concurrently. COMT and MAO are two major enzyme systems involved in metabolizing catecholamines. Combining a COMT inhibitor with a nonselective MAOI could lead to the inhibition of most of the pathways responsible for normal catecholamine metabolism. This leads to accumulation of catecholamines and sympathomimetic responses. Entacapone is a chelator of iron (DailyMed, *Entacapone,* 2022).

This class is contraindicated in clients with a history of psychotic disorder who are at risk of experiencing exacerbation of symptoms. Also, certain medications used to treat psychosis may exacerbate the symptoms of PD and decrease the effectiveness of the COMT inhibitor. This drug classification should not be stopped abruptly because it could lead to the reemergence of signs and symptoms of PD, which are sometimes worse than the initial manifestations. It could also lead to confusion, muscle rigidity, hyperpyrexia, and autonomic instability that resembles NMS.

Table 11.10 is a drug prototype table of COMT inhibitors featuring entacapone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Selective and reversible COMT inhibitors **Mechanism of Action** Prevents destruction of levodopa in the intestine and peripheral tissues Decreases production of levodopa metabolites that compete for transport across the blood–brain barrier	**Drug Dosage** Initial dose: 200 mg taken with the levodopa/carbidopa dose; can increase to a maximum of 8 doses (1600 mg/day).
Indications Adjunctive to levodopa in the treatment of PD **Therapeutic Effects** Increases the levels of levodopa that cross the blood–brain barrier, which permits more levodopa to become dopamine Prolongs the half-life of levodopa, increasing the time levodopa is available to the brain Helps to maintain stable blood levels of levodopa Improves motor function Reduces the "wearing off" time experienced during levodopa therapy	**Drug Interactions** Methyldopa Dobutamine Isoproterenol Nonselective MAOIs **Food Interactions** No significant interactions
Adverse Effects Orthostatic hypotension Dyskinesias Hepatotoxicity Hallucinations Sleep disturbances Hyperpyrexia/rigidity/confusion Nausea/vomiting/anorexia/diarrhea Brownish-orange discoloration of the urine Neuroleptic malignant syndrome	**Contraindications** Hypersensitivity to any component of drug Caution: Hypotension/orthostatic hypotension Syncope Hallucinations and psychotic-like behavior Impulse control/compulsive behavior Diarrhea/colitis Dyskinesias

TABLE 11.10 **Drug Prototype Table: Entacapone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking COMT inhibitors:

- Monitor liver enzymes at baseline and throughout therapy as recommended.
- Monitor blood pressure with position changes due to the risk of orthostatic hypotension.
- Encourage and educate the client to be compliant with the required lab testing to identify liver disease early.
- Routinely assess level of consciousness and orientation.
- Educate the client to monitor temperature periodically due to the risk of NMS.
- Specifically ask the client about feeling drowsy or sleepy while performing certain activities.
- Advise clients to exercise caution while driving, operating machinery, or working at heights.
- Ask about new or increased gambling urges, sexual urges, or uncontrolled spending.
- Monitor for melanomas frequently by performing a thorough skin assessment.
- Inform client that hallucinations and other psychotic behavior can occur.
- Explain to client that the color of the urine may become brownish orange, but this is harmless.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a COMT inhibitor should:

- Immediately notify the provider of the occurrence of right upper quadrant pain, persistent nausea, anorexia, clay-colored stools, dark urine, jaundice, fatigue, and/or lethargy.
- Notify the health care provider if they have experienced episodes of falling asleep during activities.
- Drink adequate fluids to maintain hydration if diarrhea occurs.
- Perform a routine skin assessment.

The client taking a COMT inhibitor *should not:*

- Rise or change positions quickly due to possible orthostatic hypotension.
- Stop drugs abruptly because symptoms will quickly reoccur.
- Take any sedating medications.

FDA BLACK BOX WARNING

Tolcapone

Clients who take tolcapone risk potentially fatal acute fulminant liver failure.

Dopamine Antagonists

Dopamine antagonists can help reduce symptoms of PD and levodopa-induced dyskinesia. Unfortunately, after several months, the effects of the drug wear off. This classification of drugs can be used as a monotherapy in the early stages of the disease and/or combined with levodopa/carbidopa during later stages to control dyskinesia.

Amantadine

Amantadine (Gocovri) is a second-line therapy because it is not as effective as other anti-Parkinsonian drugs. Although multiple drugs fit this classification, amantadine is the most used in PD. This drug falls into two drug classifications: antiviral and anti-Parkinsonian agent. Onset of action usually occurs within 48 hours, and it has a half-life of 10–25 hours. Because the medication is excreted unchanged in the kidneys, it may accumulate within the plasma of older adults and those with renal insufficiency. The dose should be reduced in those with renal impairment and in clients who are 65 years of age or older. This is one reason it is a second-line therapy, because older adults are more likely to have PD (DailyMed, *Amantadine*, 2023).

SAFETY ALERT

Similarly Named Drugs

Do not confuse amantadine (dopamine antagonist) with amiodarone (antiarrhythmic).

(Source: ISMP, 2023)

Adverse Effects and Contraindications

Suicidal attempts, some of which have been fatal, have been reported. The practitioner must sufficiently assess suicide risk factors and suicidal ideations before medication is prescribed. Other psychiatric manifestations caused by this drug include delirium, hypertonia, delusions, hallucinations, anxiety, euphoria, paranoia, manic reaction, and tremors. This drug can cause clients to engage in compulsive behavior and to lack impulse control. In some clients, reduction of dose or discontinuing the drug can stop these urges. Other clients may need additional help with psychotherapy. CNS stimulants can exacerbate the mental and psychiatric manifestations.

Amantadine can cause elevated levels of creatinine phosphate kinase (CPK), serum myoglobin, BUN, serum creatinine, alkaline phosphatase, low-density lipoprotein (LDL), and liver enzymes. Clients who take amantadine for more than 1 month often develop livedo reticularis, which is characterized by purple mottling of the skin. This condition is benign and gradually subsides after the drug is discontinued (DailyMed, *Amantadine*, 2023).

Abrupt discontinuation may precipitate agitation, slurred speech, depression, stupor, delirium, delusions, and hallucinations. In addition, several cases of NMS have occurred upon discontinuing the medication. This is a life-

threatening condition and immediate treatment is necessary. Clinical manifestations of this includes high fever, muscle rigidity, involuntary movements, altered consciousness, tachycardia, tachypnea, and changes in blood pressure.

The drug can exacerbate symptoms in clients with heart failure. The seizure threshold is lowered by this drug; therefore, those with seizure disorders are more apt to have frequent seizures if their medications are not adjusted.

Angle-closure glaucoma is a contraindication due to the mydriasis and further narrowing of the angle between the cornea and iris. This can worsen the glaucoma.

Table 11.11 is a drug prototype table of dopamine antagonists featuring amantadine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Dopamine antagonist **Mechanism of Action:** Increases release of dopamine from vesicles in the presynaptic neurons Blocks reuptake of dopamine into the presynaptic neurons Blocks cholinergic, NMDA, and glutamate receptors	**Drug Dosage** 100 mg capsule orally twice daily; if not adequately effective, increase to 400 mg daily in 2 divided doses.
Indications Reduction of PD symptoms Management of levodopa-induced dyskinesia **Therapeutic Effects** Decrease in tremors, bradykinesia, and rigidity Can help to reduce dyskinesias resulting from levodopa	**Drug Interactions** CNS stimulants Anticholinergics Quinidine Live vaccines **Food Interactions** No significant interactions
Adverse Effects Severe allergic reaction Suicidal thoughts Livedo reticularis Seizures NMS Orthostatic hypotension Tachypnea Anxiety/irritability/nervousness Agranulocytosis Peripheral edema Mydriasis/blurry vision Psychiatric manifestations	**Contraindications** Hypersensitivity to any component of drug Caution: Renal impairment Epilepsy Heart failure/peripheral edema Hepatic disease History of suicidal ideation or suicide attempts NMS Melanoma Impulse control/compulsive behaviors Hypotension

TABLE 11.11 **Drug Prototype Table: Amantadine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking dopamine antagonists:

- Ask about suicidal ideations, plan, and accessibility of their plan.
- Measure temperature for increases because client is at risk for infection due to reduction in white blood cell count, or it can indicate NMS.
- Monitor for an increase in respirations and heart rate as these are related to NMS.
- Assess for decreases in blood pressure upon position changes.
- Obtain a periodic ECG to monitor the QT interval.
- Assess for any seizure activity because the drug can decrease the seizure threshold.

- Perform a skin examination to monitor for melanomas.
- Specifically ask client about new or increased gambling urges, sexual urges, and uncontrolled spending.
- Monitor intake and output for a positive net result due to risk of urinary retention.
- Assess for peripheral edema, shortness of breath, and increased blood pressure.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a dopamine antagonist should:

- Immediately notify a support person or health care provider if having thoughts of harming self.
  - Caregivers should be aware of indications that client is suicidal, such as giving treasured items away, social isolation, or increased happiness (because they have made the decision to carry out their plan).
- Move and change positions slowly due to orthostatic hypotension.
- Sit or lie down if dizziness occurs and wait until it subsides before standing or walking.
- Ensure lighting is dimmed to prevent light sensitivity secondary to mydriasis.
- Maintain observation of any skin lesions to assess for changes.
- Contact the health care provider immediately if having signs of an allergic reaction, such as urticarial rash, angioedema, pharyngeal/tongue edema, and difficulty breathing.
- Gradually increase physical activity as symptoms of PD improve.
- Notify health care provider if they notice signs of mental status or mood changes, edema of extremities, shortness of breath, or difficulty urinating.
- Be observant for any impulsive spending or compulsive behavior.

The client taking a dopamine antagonist *should not:*

- Stop taking the drug abruptly to prevent Parkinsonism crisis or psychiatric manifestations.
- Overexert themselves; they should take rest periods between activities.
- Engage in driving or other tasks that require clear vision.
- Eat or drink items that can cause the urine to become acidic, such as citrus juices and fruits (lemons, grapes, grapefruits, pineapples, oranges, and blueberries).

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Marcus Bell is a 68-year-old client who arrives at the provider's office reporting a tremor in his right hand that has developed gradually over several months. He notices the tremors disappear when he is concentrating on it; however, they return quickly when he gets distracted. His wife states he has had a difficult time writing. He struggles holding the pen, and his writing is very small and sloppy. The client's wife also voiced her concerns that he never smiles anymore and he cannot keep up with her when walking. Based on the history and physical examination, the provider diagnoses Marcus with the early stages of PD. The provider prescribes carbidopa/levodopa (Sinemet) 25 mg/100 mg three times daily.

History
Benign prostatic hyperplasia
Atrial fibrillation
Osteoarthritis
Emphysema
Cataracts

Current Medications
Flomax 0.4 mg orally, once daily
Xarelto 2.5 mg orally, twice daily
Lisinopril 20 mg orally, once daily
Advair Diskus 250 mg/50 mg, inhalation, twice daily

Denies nicotine, vaping, alcohol, or illicit drug use

Vital Signs		Physical Examination
Temperature:	98.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Slight drooling but otherwise unremarkable. • *Cardiovascular:* Audible S1, S2. Rhythm irregular. Absent jugular vein distention, no peripheral edema noted bilaterally. • *Respiratory:* Clear in all fields bilaterally. Breath sounds unlabored and regular. Equal chest expansion. • *Gastrointestinal:* Abdomen flat, soft, and nontender. • *Genitourinary:* Difficulty starting urinary stream, weak flow, and dribbling afterward. Mild suprapubic distention. • *Musculoskeletal:* Stooped posture while sitting. Gait unsteady with shuffling, slow steps, and reduced arm swing. Increased muscle tone with cogwheel rigidity in upper extremities. • *Neurological:* Resting tremor in right hand. Flat affect. • *Integumentary:* Skin intact.
Blood pressure:	126/72 mm Hg	
Heart rate:	78 beats/min	
Respiratory rate:	22 breaths/min	
Oxygen saturation:	90% on room air	
Height:	5'8"	
Weight:	204 lb	

TABLE 11.12

1. After reviewing the client's history, which condition would be most concerning when starting levodopa-carbidopa?
   a. Cataracts
   b. Emphysema
   c. Atrial fibrillation
   d. Osteoarthritis

2. What medication would the nurse question if they saw it prescribed?
   a. Benztropine
   b. Entacapone
   c. Ropinirole
   d. Selegiline

11.3 Introduction to Multiple Sclerosis

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 11.3.1 Describe the pathophysiology of multiple sclerosis.
- 11.3.2 Identify the clinical manifestations related to multiple sclerosis.
- 11.3.3 Identify the etiology and diagnostic studies related to multiple sclerosis.

Multiple sclerosis (MS) is a debilitating, inflammatory, immune-mediated condition. According to the National Multiple Sclerosis Society (2023), studies have confirmed that nearly 1 million people are living with MS in the United States. This disease is characterized by a progressive and irreversible **demyelination** and axonal degeneration of the brain, spinal cord, and optic nerves. Myelin is a protective sheath that acts as an insulator of the electrical signal (see Figure 11.4). It allows rapid conduction of a nerve impulse down the axon. Degeneration of the **myelin sheath** results in the inability of nerves to conduct electrical impulses. As the myelin deteriorates, **oligodendrocytes** repair the damage but also form scar tissue called gliotic plaques. These plaques will begin to interfere with electrical impulses traveling through the axon. Over time, the myelin cannot regenerate and nerves eventually wither away. Typically, the client experiences **remissions** and **exacerbations** throughout the progression. Sensory and motor deficits become worse as the client ages. The disease is progressive and affects nerves in both the CNS and peripheral nervous system (PNS) (Capriotti, 2020).

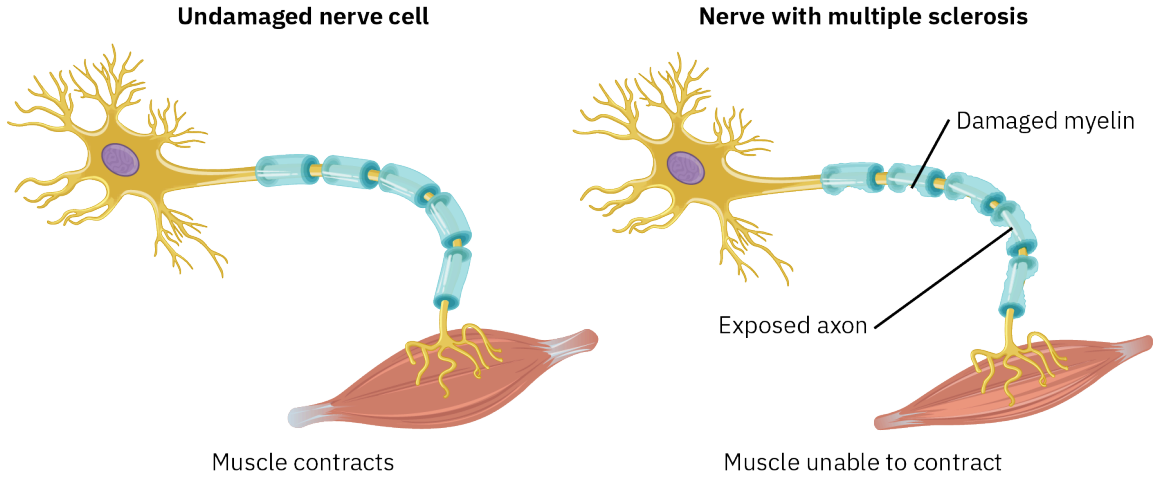


FIGURE 11.4 MS causes the protective myelin sheath and axons to degenerate, which negatively affects the transmission of nerve impulses and affects muscle contraction. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

SPECIAL CONSIDERATIONS

Age, Sex, Race/Ethnicity, and Location

- MS often presents in adults between the ages of 20 and 40 years.
- It more commonly affects females.
- It is seen more frequently in White clients than in Hispanic or Black clients.
- MS more commonly affects individuals who live farther away from the equator.

(Source: Multiple Sclerosis Foundation, 2018)

Etiology

MS is an **autoimmune** disorder that occurs when there is a malfunction of the immune system and the body mistakenly attacks its own tissue. In this case, it attacks the myelin sheath of the CNS. The exact cause of MS has not yet been fully determined; however, it is believed a combination of factors are involved. Risk factors include viral infections that theoretically mimic the components of the myelin sheath. The virus most associated with MS is the Epstein-Barr virus, which causes infectious mononucleosis. Other potential risk factors include geographic location, exposure to heavy metals, cigarette smoking (contributes to inflammation), lack of sunlight exposure, and deficient

vitamin D levels. It is believed that vitamin D can lower the risk of developing autoimmune disorders because it plays a role in immune function and regulation. Moreover, obesity is a risk factor because it contributes to long-term inflammation. Likewise, family history is shown to contribute to a person's risk of developing MS. Current research suggests there are numerous genetic variants, most of them correlating with the immune system. Some researchers believe the immune system attacks the CNS because it is simply destroying unhealthy brain cells (National Institute of Neurological Disorders and Stroke, 2023a).

Pathophysiology

Autoreactive lymphocytes mediate the destruction in MS. T-lymphocytes are sensitized and reactive to protein on the myelin sheath. These overactive immune cells cause inflammation, which begins to damage the myelin. The damage occurs in diffuse patches throughout the CNS. The damage mainly affects the white matter and results in lesions, which are called **plaques** because they are easily visible on imaging studies. Over time, hardened scar tissue develops at the lesion site, which disrupts the transmission of nerve signals. The scar tissue can slow or even stop nerve impulses altogether. Overall, signals are unable to communicate with the brain to receive information about what the body should do in situations. Other immune involvement includes **B lymphocytes**, **macrophages**, and **immunoglobulins** (IgG and IgM) as well as T-helper and T-regulator cells. The immune cells are believed to release various cytokines, such as interleukins. The blood–brain barrier becomes disrupted and oligodendrocytes, along with axons, are destroyed. The oligodendrocytes that have not been affected are incapable of adequately **proliferating**; therefore, they are ineffective in repairing the myelin. As the disease progresses, the cerebral cortex of the brain atrophies and scar tissue begins to develop (Capriotti, 2020).

LINK TO LEARNING

Living with Multiple Sclerosis

Access multimedia content (https://openstax.org/books/pharmacology/pages/11-3-introduction-to-multiple-sclerosis)

In this link to learning, Robin Brockelsby shares her story of living with MS. This video provides an overall picture of MS and how Brockelsby learned to cope with this illness.

Diagnostics

Diagnosis is sometimes delayed because there is no definitive test for MS, and many early clinical manifestations are subtle and correlate with other diagnoses. The first steps toward a diagnosis are a thorough medical history and full neurological examination. An MRI test with contrast is the most sensitive method available to identify areas of demyelination. The response of the CNS to peripheral sensory stimuli can be determined using evoked potential testing—tests that measure electrical activity in response to certain stimuli—for various pathways (visual, auditory, and sensory). Another diagnostic tool is the evaluation of the cerebrospinal fluid (CSF) obtained from a lumbar puncture. Clients with MS have high protein levels, oligoclonal bands (OCBs), IgG/IgM, and T and B lymphocytes in their CSF. Blood tests may be obtained to rule out other conditions that mimic MS or to check for risk factors, such as a vitamin D level (Capriotti, 2020).

Clinical Manifestations

The course of MS is unpredictable. Signs and symptoms vary depending on severity and the specific nerves affected by the plaque. Some clients will have very little disability, whereas others experience a steady decline with increasing disability. Fever, sun exposure, and stress can trigger exacerbations. Characteristic manifestations include:

- Sensory deficits in extremities and face (numbness and tingling sensation, itching, coldness, paralysis)
  - Some clients experience **Lhermitte sign**, an electrical shock–like sensation that runs down the back and into the limbs. This mainly occurs when the client bends their head forward.
- Visual changes (**diplopia**, **nystagmus**, unilateral vision loss, abnormal gaze, and pain with eye movement)
  - The most common and earliest symptoms are associated with the eyes.

- Motor spasticity, weakness, **ataxia**, and hyperactive reflexes
- Elimination issues (urgency, incontinence, urinary retention, constipation)
- Cognitive and mental changes (fatigue, reduced attention span, poor judgment, loss of recent memory, difficulty with abstract reasoning and solving problems—depression and anxiety are very common)
- Sexual dysfunction (decreased libido, erectile disorder, reduced genital sensation)
- Brainstem problems (**dysarthria**, **dysphagia**, weak cough)
- Pain (**neuropathic pain** in extremities, painful muscle spasms)

The most common form of MS is the relapsing-remitting form, which consists of brief episodes of several weeks to 3 months. These episodes are followed by a complete or almost complete return to baseline. The primary-progressive form does not have any remissions or exacerbations. The onset of this form is around age 40. Those with relapsing-remitting form may go on to develop secondary-progressive deterioration that leads to disabilities (Capriotti, 2020; National Institute of Neurological Disorders and Stroke, 2023a). Refer to Table 11.13 for descriptions of the various forms of MS.

Form of MS	Description
Clinically isolated syndrome (CIS)	Refers to the first episode of MS. Neurological symptoms caused by demyelination and inflammation lasting for at least 24 hours. MRI displays findings consistent with MS.
Relapsing remitting (RRMS)	Characterized by clearly defined acute attacks with full recovery. The symptoms experienced are varied and occur every 1–3 years.
Primary progressive (PPMS)	Characterized by progression of disability from the onset. There may or may not be occasional plateaus and temporary minor improvements.
Secondary progressive (SPMS)	Begins with an initial relapsing-remitting disease course, followed by progression of disability with occasional relapses and minor remissions and plateaus.

TABLE 11.13 Disease Courses of Multiple Sclerosis (source: Capriotti, 2020)

Pharmacologic Management

There is currently no cure for MS; however, the use of drugs has made a significant difference in the lives of those with MS. Most of the drugs target specific symptoms, reduce relapse rates, and delay progression. In the most common form (relapsing-remitting), early initiation of medications is highly recommended. Several drug classifications are used that work through different mechanisms: corticosteroids can reduce inflammation and speed recovery during acute exacerbations; beta interferons can slow damage; and disease-modifying agents and immunomodulators suppress the immune system to prevent the antibodies from attacking their own cells. Additionally, various components of the immune system are specifically targeted by medications. Some drugs reduce the number of T cells circulating in the periphery; others destroy target B cells or deplete B and T cells; still others prevent leukocyte mobilization to injured tissue. Drugs, such as antispasmodics, antidepressants, and antiepileptics, are prescribed to control symptoms.

Nonpharmacologic Management

Plasmapheresis (removal of abnormal antibodies) can be done for those who do not respond well to drugs. Significant nonpharmacologic management should involve teaching the client coping mechanisms, ensuring support systems are in place, and emphasizing proper nutrition and sufficient rest; the client should be encouraged to incorporate exercise into their daily routine. These actions can promote overall health, which can help the client better deal with symptoms of relapse as well as maintain their quality of life. Finally, physical therapy and occupational therapy can help to maximize functioning in various ways (National Institute of Neurological Disorders and Stroke, 2023a).

TRENDING TODAY

Advances in Multiple Sclerosis Treatment

According to the National Institute of Neurological Disorders and Stroke (2023a), researchers continue to study the mechanism of MS to identify ways to prevent or stop the continuous decline in function seen in clients with this progressive disease. Ublituximab (Briumvi) (https://openstax.org/r/tgtherapeutics) recently became the third anti-CD20 monoclonal antibody approved by the FDA as a treatment for relapsing forms of MS (Cunha, 2023). This drug is administered over 1 hour and given twice a year.

CLINICAL TIP

Treating an Acute Relapse

A short course of a high-dose intravenous (IV) glucocorticoid (e.g., 500–1000 mg of methylprednisolone daily for 3–5 days) is the preferred treatment for an acute episode. These drugs suppress inflammation and can reduce the severity and duration of an attack. When used short-term, these drugs are safe except for a possible elevation of blood glucose levels. In contrast, long-term use (e.g., over 3 weeks) can cause multiple adverse effects in numerous areas of the body, including adrenal insufficiency leading to fluid and electrolyte imbalances, osteoporosis, high risk for infections, myopathy, and psychological disturbances (agitation, anxiety, or irritability).

Acute relapse may also be treated with IV gamma globulin. This option is especially beneficial for clients who are unable to tolerant or respond adequately to glucocorticoids.

11.4 Drugs Used in the Treatment of Multiple Sclerosis

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 11.4.1 Identify the characteristics of drugs used to treat multiple sclerosis.
- 11.4.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of drugs used to treat multiple sclerosis.
- 11.4.3 Describe the nursing implications of drugs used to treat multiple sclerosis.
- 11.4.4 Explain the client education related to drugs used to treat multiple sclerosis.

Interferons

Interferons are proteins that are released in response to pathogens. Synthetic interferons have been made to resemble naturally occurring ones. These agents are important for treating viral infections, neoplasms, and autoimmune diseases such as MS. They have antiviral, antiproliferative, and immunomodulatory actions and should be used early in the disease because they have been shown to modify disease progression and reduce relapse rates. Interferon drugs are available as interferon beta-1a (given intramuscularly) and interferon beta-1b (given subcutaneously). This classification reduces the severity of symptoms and decreases the number of lesions detected with MRI. There are different mechanisms of action for interferons, including inhibition of the growth of some cells, changes in cell surface antigen expression, and induction to lymphocytic cytotoxicity.

Table 11.14 lists common interferons and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Interferon beta-1a (Avonex)	30 mcg intramuscularly weekly *or* 7.5 mcg intramuscularly weekly, then increase dose by 7.5 mcg each week until 30 mcg once weekly is reached.
Interferon beta-1b (Betaseron)	0.0625 mg subcutaneously every other day; gradually increase dose by 0.0625 mg every 2 weeks to a maximum dose of 0.25 mg every other day.

TABLE 11.14 Drug Emphasis Table: Interferons (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Avonex is produced by recombinant DNA technology using genetically engineered Chinese hamster ovary cells into which the human interferon beta gene has been introduced. Betaseron is manufactured by bacterial fermentation of a strain of *Escherichia coli* that possesses the gene for human interferon beta. In addition, the medication contains mannitol and albumin. Anyone with a hypersensitivity to any of these three components could develop angioedema or anaphylaxis (DailyMed, *Betaseron*, 2023).

Flu-like symptoms on treatment days are common when first started. Symptoms experienced are fever, chills, myalgia, malaise, and sweating. These usually diminish over time. The symptoms can be minimized by starting with a low dose and then slowly titrating up to the full dose or by giving an analgesic/antipyretic medication before taking the interferon. Neutralizing antibodies can form against synthetic agents. This will decrease the drug's effectiveness but also increase the risk of anaphylaxis.

Drug-induced lupus erythematous has been reported. Clinical manifestations include rash, polyarthritis, nephritis, and serositis. If this occurs, the drug should be stopped. Interferon beta can injure the liver by causing an asymptomatic increase in circulating liver enzymes. Liver function tests must be monitored routinely. If liver injury is evident, the dose can be decreased or a temporary interruption of treatment could be tried. When the liver function returns to baseline, treatment can resume with continued careful monitoring (DailyMed, *Betaseron*, 2023).

Transient injection site reactions include redness, pain, swelling, itching, or a lump. Injection site necrosis can occur with this drug, and some lesions have extended to the fascia overlying the muscle. Some have developed injection site abscesses and cellulitis, but this is usually the result of poor technique.

With interferon alpha, clients can develop subclinical hypothyroidism. It first causes inflammation of the thyroid (thyroiditis) that causes a short period of hyperthyroidism followed by hypothyroidism. Symptoms of heart failure can be exacerbated. Although these drugs have no direct-acting cardiac toxicity properties, they can trigger symptoms to arise.

Other immunosuppressive agents may increase the toxic effects of both immunosuppressives and elevate the risk of serious infection. Infections are related to the immunosuppressant effects. Many of these are opportunistic and are produced by microbes that do not normally cause infections unless the host is immunocompromised. Live vaccines should be avoided due to increased risk of vaccine-related infections. If needed, clients should receive them at least 4–6 weeks before starting therapy, especially the varicella-zoster virus (VZV) vaccine if one did not have chickenpox. Overall, the immunosuppression decreases the body's response to vaccines and renders them useless (DailyMed, *Betaseron*, 2023).

Table 11.15 is a drug prototype table for interferons featuring interferon beta-1b. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Interferons (biologic or synthetic) **Mechanism of Action** Enhances suppressor T-cell activity Reduces pro-inflammatory cytokine production Down-regulates antigen presentation Inhibits lymphocyte trafficking from crossing the blood–brain barrier and reaching neurons of the CNS	**Drug Dosage** 0.0625 mg subcutaneously every other day; gradually increase dose by 0.0625 mg every 2 weeks to a maximum dose of 0.25 mg every other day.
Indications Relapsing forms of MS (CIS, RRMS, SPMS) **Therapeutic Effects** Decreases frequency and severity of relapse reactions Reduces development and size of brain lesions	**Drug Interactions** Hypersensitivity to albumin, mannitol, or *E. coli*–derived products Chemotherapeutic agents Bone marrow suppressing drugs Live vaccines **Food Interactions** No significant interactions
Adverse Effects Flu-like symptoms (fever, chills, headache, myalgia) Injection site reactions Infection Anaphylaxis Neutralizing antibodies Depression/suicidal ideations/psychosis Hepatotoxicity Leukopenia/neutropenia/lymphopenia Thrombocytopenia Drug-induced lupus erythematous Hyperthyroidism/hypothyroidism (interferon alpha)	**Contraindications** Hypersensitivity to interferon beta, any ingredient within the drug, or albumin Caution: Heart failure Psychiatric conditions Thyroid disorder Depression Immunocompromised clients Active liver disease

TABLE 11.15 **Drug Prototype Table: Interferon Beta-1b** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking interferons:

- Closely examine the injection sites for redness, swelling, and/or tenderness.
- Explain to the client the importance of avoiding contact with infected or sick people.
- Monitor the following lab studies before starting the medication and periodically throughout therapy: complete blood cell count (CBC) with differential, thyroid function, and liver function tests.
- Assess for any signs of infection or excessive bleeding or easy bruising.
- Emphasize to the client to avoid injuries and apply direct pressure to the affected area for several minutes.
- Teach the client signs and symptoms of hypo- and hyperthyroidism.
- Medicate with analgesics-antipyretics on injection days to decrease flu-like symptoms.
- Evaluate for any indication of depression or suicidal ideations.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an interferon should:

- Report any signs of infection, such as a fever or sore throat.
- Avoid injuries. If one occurs, direct pressure should be applied to the affected area to control bleeding.

- Promote a balance of rest and exercise.
- Have the ability to correctly reconstitute and prepare the medication using aseptic technique.
- Rotate injection sites with each injection. The same site should not be used two consecutive times.
- Use proper technique in administering a subcutaneous injection.
- Notify the provider of feelings of depression or suicidal thoughts.
- Notify the provider of right upper quadrant pain, jaundice, dark urine, anorexia, fatigue, and clay-colored stools.
- Take an analgesic-antipyretic on the days of treatment to minimize the flu-like symptoms.
- Immediately contact the provider with the first signs of a rash.
- Contact the provider if any signs of thyroid dysfunction, such as temperature intolerances, change in weight, or level of energy, occur.

The client taking an interferon *should not:*

- Overexert themselves; they should take rest periods between activities.
- Spend time with individuals who are actively sick or spend time in crowds.
- Receive live vaccines while on therapy or within 3 months of stopping therapy.
- Inject in a site that is red, bruised, infected, scabbed, broken, or has lumps.

Immunomodulators

Immunomodulators work by blocking the activity of specific cytokines, which promote autoimmune reactions and inflammation in MS. Immunomodulators are used for treating relapsing forms of MS (RRMS and active SPMS) and reducing the frequency of relapses and slowing down the accumulation of disabilities. Common immunomodulators include:

- *Teriflunomide:* An active metabolite of leflunomide, which is a drug that was previously approved to treat rheumatic arthritis. It inhibits dihydroorotate dehydrogenase. The overall result is a reduction of the number of activated lymphocytes in the CNS. This can reduce or prevent the number of relapses a client experiences (DailyMed, *Teriflunomide*, 2023).
- *Monomethyl fumarate:* This drug inhibits immune processes that damage the brain and spinal cord; it also has antioxidant properties. Monomethyl fumarate comes in a delayed-release capsule. Certain lab tests must be obtained before initiating this drug, including CBC with differential, liver enzymes, and total bilirubin levels. A CBC with differential also needs to be obtained 6 months after the start of the medication and then every 6–12 months thereafter. Adverse reactions associated with this drug include flushing, anaphylaxis, angioedema, progressive multifocal leukoencephalopathy (PML), herpes zoster, lymphopenia, and hepatotoxicity. A non-enteric coated aspirin (325 mg or less) may be taken 30 minutes before taking the drug to reduce the incidence or severity of flushing. For the remaining adverse reactions, the drug is held and appropriate treatment given (DailyMed, *Bafiertam*, 2023).
- *Glatiramer acetate:* This drug is thought to curb the body's attack of the myelin covering by acting as a decoy to T-cell attack. Also, it induces and activates suppressor T cells in the periphery, which modifies the immune process. This drug does not cause many of the bone suppression reactions or flu-like symptoms similar to the other immunomodulators. It can cause postinjection reactions including flushing, urticaria, chest tightness, palpitations, or dyspnea. These should last only a few minutes and subside spontaneously. If symptoms last longer or are more intense, the client must notify the provider immediately (DailyMed, *Glatiramer Acetate*, 2023).

The medication must be stored in the refrigerator. Before administration, allow the medication to stand at room temperature for 20 minutes. Syringes are single-use only—any unused portion must be discarded. Injection is subcutaneously in the arms, abdomen, hips, or thighs. Injection sites should be rotated to prevent **lipoatrophy** (localized loss of fat tissue). Clients who have hypersensitivity to mannitol should avoid this drug because mannitol is part of the drug mixture.

Table 11.16 lists common immunomodulators and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Teriflunomide (Aubagio)	7 mg or 14 mg orally daily.
Monomethyl fumarate (Bafiertam)	95 mg orally twice daily for 7 days, then 2 95 mg capsules orally twice daily.
Glatiramer acetate (Copaxone)	20 mg subcutaneously once daily.

TABLE 11.16 Drug Emphasis Table: Immunomodulators (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Teriflunomide is very hepatoxic throughout therapy. If the alanine aminotransferase (ALT) amount is three times the upper normal limit on two consecutive tests, the drug must be immediately stopped, and an accelerated elimination procedure will begin. This procedure includes the administration of cholestyramine or activated charcoal for 11 days. In addition, this drug is highly teratogenic, and a negative pregnancy test must be obtained before therapy. The client should avoid pregnancy and speak with their provider if they are planning on becoming pregnant. Teriflunomide is eliminated very slowly and can take months to be fully leave the body.

Clients should be screened for latent tuberculosis (TB) before beginning therapy with immunomodulators because they have been found to activate latent TB, causing an active TB infection to develop. If found to be positive, the client must be treated for the active TB before initiating immunomodulators.

This group of drugs can cause peripheral neuropathy—either mononeuropathy or polyneuropathy. Risk factors include being older than 60 years of age, concurrent neurotoxic medications, and diabetes. Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome has been associated with the use of this drug and is characterized by multiorgan hypersensitivity. DRESS can include symptoms like fever, rash, enlarged lymph nodes, facial swelling, hepatitis, nephritis, myocarditis, or myositis. Blood pressure should be checked before therapy and periodically throughout. An elevated blood pressure should be properly managed.

Concurrent use of drugs that have immunosuppressive and/or bone marrow suppressive properties should be avoided because it can increase the risk of infections. Teriflunomide can decrease the peak international normalized ratio (INR) by 25% in clients taking warfarin. Close monitoring of the INR is warranted to evaluate for warfarin dose adjustments to maintain therapeutic levels. This drug can also reduce the effectiveness of some oral contraceptives; therefore, a second barrier backup plan should be in place. In addition, the HMG-Co-A reductase inhibitors are prevented from being metabolized and can build up in the body. Live vaccines should be avoided because they can increase the risk of infection. These vaccines should be held until 6 months after immunomodulators have been discontinued.

Table 11.17 is a drug prototype table of immunomodulators featuring teriflunomide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Immunomodulator (synthetic) **Mechanism of Action** Inhibits dihydroorotate dehydrogenase, a mitochondrial enzyme involved in pyrimidine synthesis	**Drug Dosage** 7 or 14 mg orally daily.
Indications Relapsing forms of MS (CIS, RRMS, SPMS) **Therapeutic Effects** Reduces the number of activated lymphocytes in the CNS	**Drug Interactions** Other drugs that cause immunosuppressive effects Other hepatotoxic drugs Oral contraceptives Warfarin HMG-Co-A reductase inhibitors Live vaccines **Food Interactions** No significant interactions
Adverse Effects Elevated blood pressure Anaphylaxis/angioedema Hepatotoxicity Bone marrow suppression Infections Stevens–Johnson syndrome DRESS Peripheral neuropathy	**Contraindications** Hypersensitivity Pregnancy/breastfeeding Active acute or long-term infections Severe hepatic impairment Immunocompromise

TABLE 11.17 **Drug Prototype Table: Teriflunomide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking immunomodulators:

- Monitor the following lab values at baseline and routinely during therapy: ALT, aspartate aminotransferase (AST), serum bilirubin levels, CBC with differential.
- Observe for any signs and symptoms of infection and teach the client ways to prevent infection.
- Teach clients of reproductive age that they should use an effective contraceptive barrier.
- Monitor temperature and blood pressure during therapy.
- Perform a tuberculin skin test or interferon-gamma release assay (IGRA) to rule out latent TB before drug therapy is initiated.
- Obtain a pregnancy test before the start of treatment.
- Observe for any skin rashes/reactions.
- Monitor for any signs of bleeding, such as multiple bruises, hematuria, blood in the stool, or epistaxis.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an immunomodulator should:

- Notify the health care provider if manifestations of liver injury occur, such as dark urine, clay-colored stools, right upper quadrant pain, or jaundice.
- Contact provider immediately with any evidence of infection, such as fever or sore throat.
- Notify the provider if they want to get pregnant because this drug can be harmful to the fetus.
- Monitor their blood pressure periodically because hypertension may occur.
- Immediately contact the provider for any signs of urticaria, rash, fever, dyspnea, wheezing, or swelling of

the eyes, throat, or tongue.
- Inform the provider if experiencing bilateral numbness or tingling of hands or feet.

The client taking an immunomodulator *should not:*

- Get pregnant or breastfeed while on this medication.
- Stay for long periods when there are crowds because of their decreased white blood cell count and immune response.
- Participate in activities that could cause injury and bleeding because of bone marrow suppression.

FDA BLACK BOX WARNING

Teriflunomide

Clients who take teriflunomide risk severe to fatal acute liver injury and embryofetal toxicity.

Monoclonal Antibodies

Monoclonal antibodies are derived from a single B-cell source. Cloning of individual B lymphocytes results in the production of biologically identical antibody molecules. These drugs must be administered intravenously because they are proteins and would get destroyed in the GI system if taken orally. A mouse or hamster is injected with the human antigen for the rodent to produce the desired antibody. Once the antigen is administered, the rodent's immune system mounts a response. Its B lymphocytes are stimulated to produce a specific antibody against that particular antigen. The B lymphocytes are extracted from the animal's spleen. The antibodies can then be isolated and prepared for clinical use. Because these antibodies originate from one single cell line, it is possible to design them to suppress specific components of the immune system responsible for causing tissue damage in certain conditions. The generic names of the monoclonal antibodies end in "-mab."

- *Alemtuzumab:* This agent is generally reserved for people who have had inadequate responses to two or more MS therapies. Due to its safety profile, this drug is only available through a restricted distribution program. Prescribers must be certified with the program by completing training. Clients must enroll and comply with ongoing monitoring requirements, and pharmacies must be authorized to dispense to certified facilities (DailyMed, *Lemtrada*, 2023).
- *Ocrelizumab:* This agent is indicated as a monotherapy for treating relapsing forms of MS including CIS, RRMS, and SSMS. In contrast to alemtuzumab and natalizumab, this medication is also used in the treatment of PPMS. This drug is administered via IV infusion and targets circulating CD20 markers on B lymphocytes, which produce antibodies. Clients must be premedicated with steroids and an antihistamine before each infusion to reduce infusion-related reactions. They also must be monitored during and for at least 1 hour after infusion; however, clients must be aware that reactions can occur up to 24 hours after the dose was received (DailyMed, *Ocrevus*, 2023).
- *Natalizumab:* This drug is indicated as a monotherapy for treating relapsing forms of MS including CIS, RRMS, and SSMS. This drug prevents cells of the immune system from entering the brain and spinal cord. It is very effective but is mainly used in clients who have failed first-line therapies. Only prescribers registered in the MS TOUCH Prescribing Program may prescribe this drug. Clients must read the medication guide and sign the enrollment form. The mechanism of action for natalizumab is different and complex compared with alemtuzumab. Overall, this drug demonstrates reduction of leukocyte migration into the brain and reduction of plaque formation. This results in an increase of the number of circulating leukocytes. The drug does not affect the absolute neutrophil count (DailyMed, *Tysabri*, 2023).

Table 11.18 lists common monoclonal antibodies and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Alemtuzumab (Lemtrada)	*Intravenous (IV) infusion over 4 hours for 2 or more treatment courses:* *First course:* 12 mg daily on 5 consecutive days (60 mg total). *Second course:* 12 mg daily on 3 consecutive days (36 mg total) 12 months after the first treatment. *Subsequent treatment courses:* 12 mg daily on 3 consecutive days as needed at least 12 months after the last dose course.
Ocrelizumab (Ocrevus)	300 mg IV infusion, followed 2 weeks later with a second 300 mg IV infusion. Subsequent doses: 600 mg IV infusion every 6 months.
Natalizumab (Tysabri)	300 mg IV over 1 hour every 4 weeks.

TABLE 11.18 **Drug Emphasis Table: Monoclonal Antibodies** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Alemtuzumab must be administered in a certified health care setting with appropriate equipment to manage anaphylaxis or other serious infusion reactions, such as myocardial ischemia, myocardial infarction, ischemic/hemorrhagic stroke, and cervicocephalic arterial dissection. These can occur following any of the doses being given. To reduce infusion-related adverse effects, clients should be premedicated with high-dose corticosteroids for the first 3 days of each treatment course. They can also receive antihistamines and/or antipyretics before the dose. Additionally, antiviral agents should be administered for herpetic prophylaxis starting on the first day of dosing and continue for a minimum of 2 months after completion of alemtuzumab dosing or until the CD4+ lymphocyte count is less than 200 cells/microliter.

Some autoimmune disorders caused by alemtuzumab include immune thrombocytopenia (spontaneous bleeding, petechiae, heavy menstrual bleeding, hemoptysis), glomerular nephropathies (edema, decreased urine output, hematuria), autoimmune hemolytic anemia (chest pain, jaundice, dark urine, tachycardia), and thyroiditis.

Clients of childbearing age should consistently use effective contraception during therapy and for 4 months after a course of treatment. This drug can cause fetal harm.

A few infections caused by alemtuzumab include hepatitis, human papilloma virus (HPV), TB, and fungal infections, especially oral and vaginal candidiasis. Any client with active disease of these infections should not take the monoclonal antibodies. Pregnant or breastfeeding clients should avoid monoclonal antibodies.

The FDA recommends that 6 weeks before starting therapy, clients should be vaccinated for VZV. No live-virus vaccines should be received after starting monoclonal antibodies.

Oletuzemab can cause immune-mediated colitis characterized by diarrhea (DailyMed, *Ocrevus*, 2023). Other ADRs, contraindications, and cautions are similar to alemtuzumab.

Table 11.19 is a drug prototype table for monoclonal antibodies featuring alemtuzumab. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Monoclonal antibodies (biologic) **Mechanism of Action** Targets CD52 protein, a cell surface antigen present on lymphocytes, natural killer cells, monocytes, and macrophages; after binding on the cell surface of lymphocytes, an antibody-dependent cellular cytolysis occurs	**Drug Dosage** *IV infusion over 4 hours for 2 or more treatment courses:* *First course:* 12 mg daily on 5 consecutive days (60 mg total). *Second course:* 12 mg daily on 3 consecutive days (36 mg total) 12 months after the first treatment. *Subsequent treatment courses:* 12 mg daily on 3 consecutive days as needed at least 12 months after the last dose course.
Indications Reduces frequency and severity of relapses in RRMS and SSMS **Therapeutic Effects** Depletes circulating T and B lymphocytes after each treatment course, resulting in less myelin sheath being destroyed	**Drug Interactions** Antineoplastics Immunosuppressive/immunomodulators **Food Interactions** No significant interactions
Adverse Effects Nasopharyngitis/URI/sinusitis Infusion reactions Stroke Increased risk of thyroid cancer and cutaneous melanomas Autoimmune disorders PML	**Contraindications** Hypersensitivity or anaphylactic reaction to alemtuzumab or any of its components HIV infection Active infection Pregnancy Active hepatitis B History of life-threatening infusion reactions Caution: Viruses Preexisting or ongoing malignancy

TABLE 11.19 **Drug Prototype Table: Alemtuzumab** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following when administering monoclonal antibodies:

- Obtain and analyze CBC with differential, serum creatinine levels, thyroid function, and urine cell count before therapy and then regularly until 48 months after last infusion.
- Obtain urine protein to creatinine ratio before the start of therapy.
- Assess client during and for 2 hours after each infusion, including vital signs, to identify any infusion-related adverse effects.
- Educate client regarding the drug's increased risk of malignancies, including thyroid cancer, melanoma, and lymph disorders.
- Teach client signs and symptoms of hypothyroidism and hyperthyroidism.
- Perform a tuberculin skin test and HPV screening.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a monoclonal antibody should:

- Be compliant related to the required monthly laboratory testing.
- Complete any necessary immunizations at least 6 weeks before treatment starting.

- Be screened for TB and HPV (if applicable).
- Understand clinical manifestations related to certain autoimmune disorders caused by therapy, such as hematuria, hemoptysis, easy bruising, petechiae, edema, decreased urine output, spontaneous bleeding, abdominal pain, and jaundice.
- Be able to differentiate manifestations related to hypo- and hyperthyroidism.
- Be able to verbalize possible signs/symptoms of stroke, such as facial droop, dysarthria, unilateral weakness, or sudden severe headache.
- Notify the provider with any indication of infection, such as fever, fatigue, sore throat, enlarged lymph nodes, or coughing.

The client taking a monoclonal antibody *should not:*

- Stop drugs abruptly because symptoms will quickly reoccur.
- Overexert themselves; they should take rest periods between activities.
- Engage in activities that could cause injury.

FDA BLACK BOX WARNING

Monoclonal Antibodies

Alemtuzumab may cause life-threatening autoimmune conditions, such as immune thrombocytopenia, serious infusion reactions resulting in anaphylaxis, potential fatal strokes, and an increase risk of malignancies.

Natalizumab may cause increased risk of PML, which is a potentially fatal viral infection of the brain.

Sphingosine 1-Phosphate Receptor Modulators

Sphingosine 1-phosphate (S1P) receptor modulators regulate immune activity by specifically blocking the activity of S1P receptors found on the surface of lymphocytes. This prevents the lymphocytes from leaving the lymph nodes and entering the bloodstream, thus reducing their activity in the CNS. S1P receptor modulators are oral drugs prescribed for RRMS and active SPMS. There are currently three drugs on the market that fit into this category. This chapter will only focus on siponimod fumaric acid (Mayzent) because there are very few differences among them. The drug is associated with a CYP2C9 genotype variant that alters the dose.

Adverse Effects and Contraindications

Initiation of S1P drug therapy results in a decrease in heart rate, for which monitoring is recommended. The nurse should administer the first dose in a setting in which resources to appropriately manage symptomatic bradycardia are available. Before dosing and at the end of the observation period, an ECG should be obtained for all clients. Observation of clients overnight is necessary if they are at higher risk of symptomatic bradycardia, heart block, prolonged QTc interval, or if taking drugs with known risk of torsades de pointes. If post-dose symptomatic bradycardia occurs, appropriate management should be initiated, beginning with continuous ECG monitoring and continuing until the symptoms have resolved.

Another adverse effect is macular edema. Fundoscopic examinations are essential before and 3–4 months after the treatment has been started. They are also performed again whenever a client reports visual disturbances. Diabetes mellitus and uveitis increase the risk of macular edema.

S1P receptor modulators may also cause fetal harm. Advise clients of childbearing age of the potential risk to a fetus and to use an effective method of contraception during treatment and for 10 days after stopping the drug.

Furthermore, siponimod fumaric acid can cause an increase in blood pressure readings. Blood pressure should be monitored routinely, and any significant changes should be reported to the provider. Suspicious skin lesions should be evaluated because the risk of basal cell carcinoma and melanoma is increased in clients being treated with siponimod fumaric acid.

There have been reported cases of posterior reversible encephalopathy syndrome (PRES) in clients receiving an S1P receptor modulator. This is caused by swelling and narrowing of the blood vessels within the brain. If a client

complains of a sudden onset of a severe headache, altered mental status, vision changes, or seizure activity, the provider should promptly schedule a complete physical and neurological examination and consider an MRI. Symptoms are usually reversible but may evolve into ischemic stroke or cerebral hemorrhage. Delay in diagnosis and treatment may lead to permanent neurological sequelae. If PRES is suspected, the drug should be discontinued.

Before initiation of treatment with siponimod fumaric acid, clients should be tested to determine their CYP2C9 genotype. Substantially elevated siponimod plasma levels may occur in clients who are homozygous for CYP2C9*3, so its use is contraindicated in these individuals.

This therapy can cause a dose-dependent reduction in peripheral lymphocyte count to 20%–30% of baseline values because of reversible sequestration of lymphocytes in lymphoid tissues. It is important not to start therapy in clients with active infection.

Avoid live vaccines during therapy and for 4 weeks after to prevent the possibility of developing an infection. Concurrently taking antineoplastics or immunosuppressive or immune-modulating therapies can elevate the client's risk of infection. Class Ia or Class III antiarrhythmic drugs should be avoided due to the increased risk of prolongation of the QTc interval. The administration of drugs that slow the heart rate or decrease atrioventricular conduction (e.g., beta blockers, digoxin, diltiazem, or verapamil) can intensify the risk of dysrhythmias or atrioventricular block or can exacerbate manifestations of heart failure. Monitor for the development of severe increase in disability following drug discontinuation and begin appropriate treatment as needed.

Table 11.20 is a drug prototype table for S1P receptor modulators featuring siponimod fumaric acid. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class S1P receptor modulator **Mechanism of Action:** Modulates its role in immune cell trafficking through sequestration of autoreactive lymphocytes in the lymphoid organs to reduce their recirculation and subsequent infiltration into the CNS	**Drug Dosage** The dosage has a 5-day titration schedule: First 2 days: 0.25 mg orally daily. Day 3: 0.5 mg orally daily. Day 4: 0.75 mg orally daily. Day 5 and maintenance dose: 1.25 mg orally daily.
Indications Reduces relapse in RRMS and SPMS Reduces symptoms in CIS **Therapeutic Effects** Regulates lymphocyte traffic by preventing lymphocytes from lymphoid organs from entering the lymphatic circulation, presumably limiting inflammatory cell migration into the CNS	**Drug Interactions** Hepatotoxic drugs Class Ia or Class III antiarrhythmic drugs Antineoplastics Immunosuppressive or immune-modulating therapies Live vaccines Drugs that slow heart rate or atrioventricular conduction (e.g., beta blockers, digoxin, diltiazem, or verapamil) **Food Interactions** No significant interactions
Adverse Effects Headache Cough/influenza/sinusitis Bradycardia/AV block Hypertension Heart failure Hepatotoxicity Severe increase in disability with MS exacerbations when discontinued Infections PML Macular edema PRES Skin malignancies Decline in pulmonary function	**Contraindications** CYP2C9 genotype In the past 6 months: • Unstable angina • Myocardial infarction • Transient ischemic attack/stroke • Class III/IV heart failure • Mobitz II or third-degree heart block Active infections Caution: Bradydysrhythmias/AV conduction delays Elevated blood pressure Liver injury

TABLE 11.20 **Drug Prototype Table: Siponimod Fumaric Acid** (sources: Roy et al., 2021; https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following when administering S1P receptor modulators:

- Before starting treatment, obtain serum transaminases (ALT and AST), total bilirubin, CBC, and pulmonary function (e.g., spirometry) if indicated.
- Before starting treatment, determine whether clients are taking drugs that could slow their heart rate or atrioventricular (AV) conduction. Obtain cardiologist consultation before concomitant use with other drugs that decrease heart rate.
- Monitor all clients for 6 hours after the first dose for signs and symptoms of bradycardia with hourly heart rate and blood pressure measurement. Provider must assess for elevated blood pressures. Clients should know ahead of time they will be in the office for a minimum of 6 hours.
- Perform a thorough skin assessment periodically for signs of malignancy, such as asymmetry, indistinct borders, color variations, and increased size and elevation of any lesions.
- Assess for any neurological changes that could be related to PRES.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an S1P receptor modulator should:

- Call provider with any dizziness, lightheadedness, shortness of breath, and fatigue.
- Notify the provider with any visual changes.
- Inform the provider of manifestations related to liver injury, such as jaundice, nausea, right upper quadrant pain, dark urine, and clay-colored stools.
- Implement measures to avoid being exposed to infection. Contact provider if signs/symptoms of infection are present.
- Limit exposure to sunlight and ultraviolet light by wearing protective clothing and using a sunscreen with a high protection factor.

The client taking an S1P receptor modulator *should not:*

- Stop drugs abruptly because symptoms will quickly reoccur.
- Ignore any suspicious skin changes, such as a newly developed lesion, change of appearance in a mole, a new darkened area on their skin, a sore that does not heal, or growths on their skin.
- Chew, split, break, or crush medication.

Muscle Relaxants

Muscle spasticity is the result of damage to neurons within the CNS rather than injury to the peripheral structures. Clients often report stiffness and/or heavy muscles, difficulty with movement, and pain. Because the nerve damage originates in the CNS, the risk of this becoming permanent is high. Spasticity results in the excessive stimulation of muscles (hypertonia) in opposing muscle groups at the same time. The different types and brands of skeletal muscle relaxants work in different ways to affect muscle function. Most are CNS depressants and prevent the nerves from sending pain signals to the brain. They have no direct effect on skeletal muscle. Other actions may include the blockage of nerve impulses that cause increased muscle tone and contraction (Cleveland Clinic, 2023).

Centrally Acting Muscle Relaxant

Along with treating spasticity, baclofen is helpful in treating pain from trigeminal neuralgia that occurs in MS. This drug is available in oral and intrathecal (within the spine) forms and can be administered through an implantable delivery pump for treating central spasticity. The drug has no direct effect on skeletal muscle; therefore, it does not reduce muscle strength.

Peripherally Acting Muscle Relaxant

Dantrolene acts peripherally on the muscle itself. The drug inhibits the release of calcium from the sarcoplasmic reticulum directly within skeletal muscle cells. This action prevents the muscle fibers from contracting. Dantrolene does not interfere with neuromuscular transmission but does impair muscle strength. This drug is also used in the treatment and prevention of malignant hyperthermia (manages muscle contraction and rigidity). This agent is not therapeutic for treating muscle spasms associated with muscle injury or rheumatic disorders (DailyMed, *Dantrolene,* 2022).

Table 11.21 lists common muscle relaxants and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Baclofen (Lioresal)	*Oral:* Start at low doses and increase gradually until optimum effect is achieved. Initial dose: 5 mg orally 3 times daily. Usually, the drug is increased by 5 mg every 3 days until desired effect is obtained. Average dose range: 40–80 mg daily. Maximum dose: 80 mg daily. *Intrathecal pump:* Start with a 100 mcg IV bolus. Maintenance therapy is individualized; generally, 300–800 mcg daily.
Dantrolene sodium (Dantrium)	25 mg daily for 7 days, then 25 mg 3 times daily for another 7 days. Increase by 25 mg every 7 days until the maximum of 100 mg 3 times daily is reached.

TABLE 11.21 **Drug Emphasis Table: Muscle Relaxants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

The most common adverse effects for baclofen are related to CNS depression. Constipation and urinary retention are linked to CNS depression of the parasympathetic nervous system reflexes. This slows down peristalsis and relaxes the detrusor muscle of the bladder. Baclofen crosses the placenta and enters breast milk, so a fetus/infant may develop CNS depression.

Cardiac concerns, such as heart failure and arrhythmias, result from the depression of the normal reflex arcs. This drug could exacerbate heart failure due to depressed muscle function caused by these drugs.

If the oral version of baclofen is stopped too quickly, this can cause the development of psychoses, visual hallucinations, and seizures. The drug should be tapered off over a 1- to 2-week period. Abrupt withdrawal of the intrathecal route can be more dangerous. Possible reactions include high fever, altered mental status, rebound spasticity, and muscle rigidity that could lead to muscle breakdown (rhabdomyolysis).

Blocking the spasticity associated with movement, posture, or balance results in loss of these functions. This places clients at high risk for falls.

Some common adverse reactions for dantrolene include diarrhea and abdominal cramps. Clients with respiratory depression must be closely monitored because this can be exacerbated by muscular weakness. Dose-related hepatotoxicity is the most serious adverse effect. Baseline liver enzymes should be obtained and monitored periodically throughout treatment. If clients show no response within 45 days of initiating this drug, it should be stopped to prevent damage to the liver. Caution should be used in all clients older than 35 years of age due to their increased risk of potentially fatal hepatocellular disease. Supplemental estrogen increases the incidence of hepatocellular toxicity. This drug should be discontinued at the first indication of hepatic impairment (DailyMed, *Baclofen*, 2023).

Table 11.22 is a drug prototype table for muscle relaxants featuring baclofen. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Centrally acting muscle relaxant **Mechanism of Action** Inhibits GABA receptors located on the spinal cord Restricts calcium influx, reducing presynaptic neurotransmitter release in the excitatory spinal pathways Reduces nerve impulse transmission from the spinal cord to the skeletal muscle, resulting in decreased muscle spasticity	**Drug Dosage** *Oral:* Start at low doses and increase gradually until optimum effect is achieved. Initial dose: 5 mg orally 3 times daily. Usually, the drug is increased by 5 mg every 3 days until desired effect is obtained. Average dose range: 40–80 mg daily. Maximum daily dose: 80 mg. *Intrathecal pump:* Start with a 100 mcg IV bolus. Maintenance therapy is individualized; generally, 300–800 mcg daily.
Indications Reversible muscle spasticity associated with neuromuscular diseases such as MS and spinal cord injuries **Therapeutic Effects** Suppresses hyperactive reflexes involved in regulating muscle movement Alleviates signs and symptoms of spasticity, especially reducing discomfort and rigidity	**Drug Interactions** Agents that cause CNS depression Alcohol Anticholinergic agents **Food Interactions** No significant interactions
Adverse Effects Weakness/drowsiness/fatigue Confusion/headache/insomnia Nausea/vomiting/constipation Urinary retention Hypotension Arrhythmias	**Contraindications** Hypersensitivity to drug or any of its ingredients Caution: Skeletal muscle spasms resulting from rheumatic disorders Spasticity that contributes to locomotion, upright position, or balance Pregnancy and breastfeeding Older adults History of schizophrenia or psychosis Heart failure BPH

TABLE 11.22 **Drug Prototype Table: Baclofen** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking muscle relaxants:

- Assess alertness, orientation, and affect.
- Evaluate muscle strength before and after administration of medication.
- Auscultate bowel sounds and monitor bowel movements due to constipation and to avoid a fecal impaction.
- Obtain baseline liver function tests and serum BUN/creatinine levels and assess these levels periodically during therapy to assess for changes.
- Ensure safety precautions are in place to prevent falls because of fatigue, weakness, and confusion.
- Provide additional measures to relieve discomfort such as heat, rest, NSAIDs, and positioning to augment effects of the drug.
- Emphasize to the client/caregiver that the drug must be gradually discontinued over a 1- to 2-week period.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a muscle relaxant should:

- Eat plenty of fruits, vegetables, and whole grains to prevent or reduce constipation.
- Drink at least 6–8 8-oz of water daily to promote regular bowel movements.
- Have a clear understanding of the baclofen pump if applicable, such as frequent monitoring, adjusting the dose, and programming the unit, to avoid complications.
- Report painful or frequent urination, constipation, headache, insomnia, or excessive fatigue.
- Understand various nonpharmacological comfort measures to use, such as heat, rest, or position change, to help relieve discomfort.
- Notify provider if signs or symptoms of liver dysfunction appear, such as right upper quadrant pain, jaundice, dark urine, and clay-colored stools.

The client taking a muscle relaxant *should not*:

- Chew, break, or crush extended-release capsules.
- Rise or change positions quickly due to possible orthostatic hypotension.
- Drive or engage in potentially hazardous tasks that require alertness and focus until the effects of the drug are known.
- Stop the drug abruptly, to prevent negative effects.

FDA BLACK BOX WARNING

Muscle Relaxants

Dantrolene sodium can cause severe to fatal hepatotoxicity, especially if taking greater than 800 mg/day.

Baclofen: Abrupt discontinuation of baclofen can cause high fever, altered mental status, and muscular changes that can result in organ failure and death.

Gamma-Aminobutyric Acid Structural Analogs

Seizures may be slightly more common in people with MS due to the way the condition affects the brain. MS damages several parts of the brain, which can lead to disruptions in signal transmission. The scar tissue of an MS lesion creates a barrier to the transmission of nerve signals down a path. The flow of the nerve signals gets redirected. If the lesions create enough barriers, the result is an abnormal discharge of excessive electrical energy from the nerve cells of the brain. Clinical manifestations vary depending on the area of the brain affected.

There are various forms of seizures. Some stimulate motor nerves, whereas others affect autonomic and sensory nerves (Moreo & Benbadis, 2019). The form a particular seizure takes depends on the cell location that initiated the electrical discharge and the neural pathways stimulated by that initial impulse. In general, the three main categories of seizures are generalized, focal, and combined. The combined form is referred to as a focal to bilateral seizure where the impulse initiated in one area of the brain and then spread to both hemispheres (secondary generalized seizure). For a more detailed discussion on the different types of seizures and their treatment, refer to Anticonvulsant Drugs and Drugs to Treat Epilepsy, Migraine Headaches, and Intracranial Emergencies.

Drugs used for seizures do not treat the underlying cause but simply control the seizure activity and modulate the inhibitory neurotransmitter GABA.

- *Gabapentin:* FDA-approved agent used as an adjunct in treating focal seizures. It is believed to enhance the release of GABA. It does not bind directly to GABA receptors. It is also helpful in the treatment of central pain caused by damage to the brain and/or spinal cord. In addition, it is used in the management of postherpetic neuralgia and restless leg syndrome. It is important to know that the forms of gabapentin indicated for these last two conditions are not equivalent with each other or that which is used for seizures (DailyMed, *Gabapentin,* 2023).

- *Pregabalin:* Approved as an adjunct in treating focal seizures, it is also FDA-approved for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia along with fibromyalgia. This drug has a high binding affinity for voltage-gated calcium channels in the cerebrovascular system. It does not bind to GABA or benzodiazepine receptors; therefore, its effect is indirect. Pregabalin is regulated under the Controlled Substances Act. It is listed as a Schedule V agent (DailyMed, *Pregabalin,* 2022).

Table 11.23 lists common GABA structural analogs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Gabapentin (Neurontin)	300 mg 3 times daily. Increase at weekly intervals as necessary. Maximum dose: 3600 mg daily.
Pregabalin (Lyrica)	*Immediate release:* 300–600 mg daily in divided doses. *Controlled release:* 165 mg daily.

TABLE 11.23 Drug Emphasis Table: GABA Structural Analogs (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Hypersensitivity reactions have occurred with GABA structural analogs. Angioedema is characterized by swelling of the face, tongue, lips, gums, throat, and larynx. The drug should immediately be discontinued at the first sign of angioedema or other hypersensitivity reaction, such as hives, rash, wheezing, or dyspnea. Weight gain, due to an increased appetite, can be significant; some clients gain 7% or more in a few months. There is a possibility of rhabdomyolysis, so clients should be taught to let the provider know if muscle pain/tenderness occurs. Decreased sperm counts, reduced sperm motility, and increased sperm abnormalities can occur in male clients taking the drug. Clients may develop a low platelet count (thrombocytopenia).

Also, it has been reported pregabalin causes subjective effects similar to diazepam, increasing the risk of physical dependence. To avoid withdrawal symptoms, such as headache, diarrhea, or insomnia, the drug should be discontinued over at least 1 week.

CNS depressants and alcohol can increase the depressant effects of pregabalin. Taking angiotensin-converting enzyme (ACE) inhibitors concurrently increases the risk of swelling and hives. If taking thiazolidinediones with pregabalin, there is a higher chance of weight gain or swelling of one's hands or feet.

Table 11.24 is a drug prototype table for GABA structural analogs featuring pregabalin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class GABA structural analogs/antiseizure **Mechanism of Action:** Binds with calcium channels on nerve terminals and can thereby inhibit neuronal calcium influx, thus decreasing the release of several neurotransmitters that may underlie seizure activity	**Drug Dosage** *Immediate release:* 300–600 mg orally daily in divided doses. *Controlled release:* 165 mg orally daily.
Indications Focal seizures Neuropathic pain **Therapeutic Effects** Modulates the calcium function in neurons, leading to a decrease in cellular excitation	**Drug Interactions** CNS depressants (benzodiazepines, opioids) Alcohol ACE inhibitors Thiazolidinediones (rosiglitazone/pioglitazone) **Food Interactions** No significant interactions
Adverse Effects CNS depression Dizziness/confusion/headaches Angioedema Increased suicidal ideations Thrombocytopenia Peripheral edema/weight gain Euphoria Decreased male fertility	**Contraindications** Hypersensitivity Caution: Clients with a history of substance or alcohol use disorders Class III/IV heart failure

TABLE 11.24 **Drug Prototype Table: Pregabalin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking GABA structural analogs:

- Ensure the client is taking an additional antiseizure medication because these are used only as adjuncts.
- Instruct the client not to break, chew, or crush the extended-release forms.
- Watch for any mood or personality changes and signs of suicidal ideation.
- Assess for seizure activity and ensure seizure precautions are in place.
- Evaluate for CNS depression to maintain client safety.
- Monitor weight and presence of peripheral edema.
- Emphasize to client not to stop drug abruptly.
- Assess client for muscle pain or tenderness.
- Monitor platelet count and creatinine kinase enzymes if muscle pain occurs.
- Evaluate history of drug use disorder or drug misuse.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a GABA structural analog should:

- Sit or lie down if excessive fatigue occurs and wait until it subsides.
- Weigh themselves at the same time each day and notify provider if they gain more than 2 pounds within 24 hours.
- Know there is a risk of dependence.
- Immediately stop the drug if any manifestations of hypersensitivity arise to prevent reaction from worsening.

- Be aware of the increased risk of suicidal thoughts and behavior.
- Notify the provider if they are experiencing muscle discomfort.
- Contact the health care provider if they notice easy bruising, prolonged bleeding, or anemia.
- Use condoms to prevent pregnancy.

The client taking a GABA structural analog *should not:*

- Stop drugs abruptly when discontinuing because there is a risk of precipitating seizures with sudden withdrawal.
- Drink alcohol due to additive sedative effects and risk for injury.
- Drive or perform tasks requiring alertness, coordination, or physical dexterity until the effects of the drug are known.
- Engage in activities or tasks that have a high risk of bleeding.

Chapter Summary

This chapter discussed the disease processes and drug classifications used in managing two progressive neurodegenerative conditions: Parkinson's disease and multiple sclerosis. There are similarities and differences among these conditions. Both cause motor and autonomic system manifestations, and neither has an identified cure. Both diseases are diagnosed mainly by clinical presentation. Medications are essentially beneficial in reducing symptoms of these conditions. In addition, medications are helpful in preventing relapses in MS and delaying the progression of PD.

The medications for each condition are distinct based on the etiologies. In PD, the medications are focused on increasing dopamine levels in the CNS by using dopamine replacement/dopamine agonist agents. Also, drugs that inhibit enzymes that metabolize the levodopa in the periphery—MAO and COMT inhibitors—are used so more dopamine reaches the CNS. Anticholinergic agents can be used as a second-line therapy in PD to decrease the unopposed ACh levels that cause many symptoms. In contrast, the overall purpose of medication in MS is to alter the immune system components to prevent further attack and damage. Generally, these are considered immunomodulators or have immunosuppressant properties. Drugs such as glucocorticoids or immunoglobulins are used in acute episodes to reduce severity and duration of the relapse. Importantly, varied classifications are necessary to treat nonmotor symptoms, such as spasticity and seizures. Overall, the main outcome for both conditions is for the client to continue to be independent as long as possible.

Key Terms

akathisia psychomotor restlessness; an intense sensation of uneasiness or inner restlessness that usually involves the lower extremities and results in a compulsion to move

alpha-synuclein neuronal protein that regulates synaptic vesicle coordination and subsequent neurotransmitter release

anhidrosis lack of sweating due to decreased sweat glands

ataxia impaired balance and coordination that can affect any part of the body and speech

atrophy decrease in size or waste away, especially as a result of cellular degeneration

autoimmune when the body's immune system cannot tell the difference between its own cells and foreign cells, the immune components mistakenly attack healthy body cells

ballismus rapid, involuntary jerking or flinging of proximal muscle groups

bradykinesia slowness of movement or progressive hesitations

catecholamine monoamine neurotransmitters released in response to physical or emotional stress (e.g., epinephrine, dopamine)

choreoathetosis slow, involuntary, writhing movements

demyelination damage to the myelin sheath that results in slowing or stopping of nerve impulses, leading to neurological problems

diplopia double vision—seeing two of the same image

dysarthria difficulty with formulating words to speak

dyskinesia abnormality or impairment of voluntary movement

dysphagia difficulty swallowing

dystonia movement disorder where muscles contract involuntarily, causing repetitive or twisting movements

exacerbation increase in the severity of a disease or its signs and symptoms

immunoglobulins glycoprotein molecules produced by B lymphocytes (plasma cells) that act as a critical part of the immune response by specifically recognizing and binding to particular antigens and aiding in their destruction

Lhermitte sign transient electric shock sensation down the spine and extremities caused by neck flexion; most notably caused by MS

lipoatrophy localized loss of adipose tissue

lymphocyte type of white blood cell that plays an essential role in the immune response (B and T lymphocytes); made in the bone marrow and found in the blood and lymph tissue

macrophages large, specialized connective tissue cells that recognize, engulf, and destroy target cells

micrographia handwriting that is very small

myelin sheath protective insulated covering surrounding nerve fibers in the brain, spinal cord, and optic nerves

neuroleptic malignant syndrome (NMS) a potentially life-threatening condition characterized by symptoms of confusion or altered mental states, muscle rigidity, hyperthermia, arrhythmias, and autonomic instability

neuropathic pain pain that originates within the CNS or PNS resulting from damage or disease

nystagmus involuntary oscillating eye movements

that are usually rapid, repetitive, and uncontrolled

oligodendrocytes type of non-neuronal cells in the CNS that do not produce electrical impulses; main functions are to provide support and insulation to axons in the CNS

Parkinson's disease (PD) a progressive neurologic condition that destroys the pigmented dopaminergic neurons of the substantia nigra

plaques deposits of neuron fragments surrounding a core of fibrillary amyloid beta-protein

progressive multifocal leukoencephalopathy (PML) opportunistic, life-threatening viral infection of the brain caused by the John Cunningham virus

proliferating multiplying or increasing in number

remissions decrease in or disappearance of signs and symptoms

rigidity continuous involuntary sustained muscle contraction that when passively stretched, the degree of resistance remains constant

tardive dyskinesia movement disorder characterized by uncontrollable, abnormal, and repetitive movements of the face, torso, and/or other body parts

Review Questions

1. A 68-year-old diagnosed with Parkinson's disease is taking entacapone in addition to carbidopa/levodopa. Which of the following would be a priority nursing intervention?

a. Check the client's blood pressure twice a day to make sure it is not elevated.
b. Assess the client's ability to independently carry out their activities of daily living.
c. Explain to the client the entacapone should be separated from the carbidopa/levodopa by 2 hours.
d. Instruct the client to report brownish-orange urine to their health care provider immediately.

2. The nurse is caring for a client who was recently diagnosed with PD. The provider wanted to begin the client on pramipexole, but the client has difficulty swallowing medications due to a previous stroke. What other medication in the same class would *best* meet the client's needs?

a. Ropinirole ER
b. Rotigotine
c. Apomorphine
d. Bromocriptine

3. An 18-year-old is having surgery on their fractured hip after a football injury. During surgery, they develop a fever of 105°F and their muscles become rigid. Which of the following medications would the nurse expect to be administered?

a. Gabapentin
b. Baclofen
c. Dantrolene
d. Pregabalin

4. The nurse is caring for a client with the primary-progressive form of multiple sclerosis (PPMS). The nurse expects which of the following drugs to be included in the treatment plan?

a. Alemtuzumab
b. Natalizumab
c. Ocrelizumab
d. Siponimod

5. A client is complaining of not being able to sleep for the past week. They mention starting a new medication at that time. Which medication could be the cause of their inability to sleep?

a. Selegiline
b. Entacapone
c. Pramipexole
d. Benztropine

6. The nurse is caring for a client who is going to begin therapy with the immunomodulator teriflunomide. Which test is important to have done before the drug is started?

a. Serum creatinine
b. Hemoglobin A1C
c. Tuberculin skin test
d. Liver function test

7. A nursing student is preparing a teaching plan for a client with PD who is being treated with carbidopa/levodopa. Which of the following dietary recommendations is correct?
a. Intake of green, leafy vegetables should be limited.
b. Daily required protein intake should be divided equally among three meals.
c. A high-fat diet will interfere with the absorption of carbidopa/levodopa.
d. High-fiber products will cause diarrhea.

8. The nurse is reviewing discharge instructions with a client with a new prescription for pregabalin. Which of the following points should be included in this discussion?
a. Weight loss is noted with prolonged use.
b. The drug is a first-line treatment for seizure disorders.
c. Improvement in suicidal ideation is common.
d. Altered impulse control can result at therapeutic doses.

9. The nurse is preparing medications for assigned clients. The nurse calls the prescriber concerned about administering benztropine to one of the clients. What would be the reason for the concern?
a. 58-year-old with diarrhea
b. 66-year-old with urinary incontinence
c. 84-year-old with glaucoma
d. 74-year-old with symptomatic bradycardia

10. Which class of drugs may reduce the therapeutic effects of levodopa if given concurrently?
a. First-generation antipsychotics
b. Selective serotonin reuptake inhibitors
c. Tricyclic antidepressants
d. Sympathomimetics

CHAPTER 12

Anticonvulsant Drugs and Drugs to Treat Epilepsy, Migraine Headaches, and Intracranial Emergencies

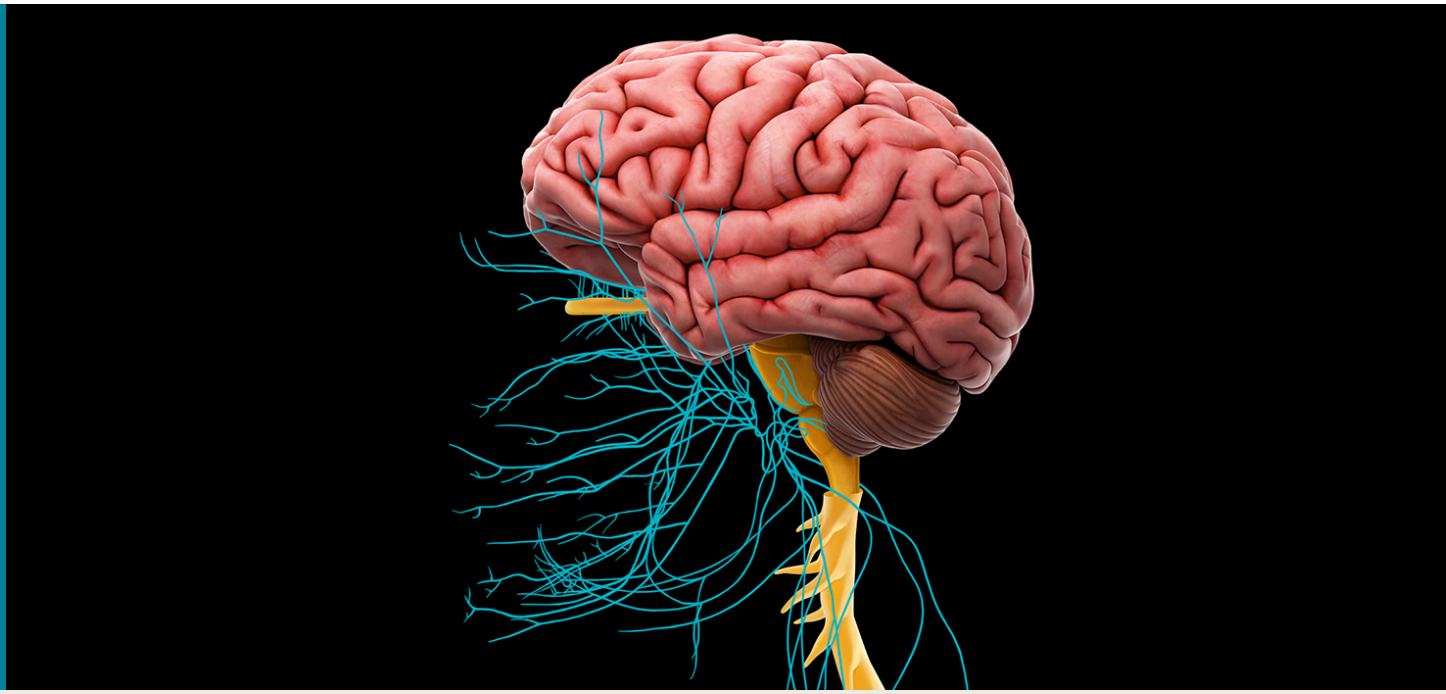


FIGURE 12.1 The nervous system, the body's control center, consists of the brain, the spinal cord, and a very complex system of nerves. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The brain, one of the most important organs of the body, controls and coordinates all bodily functions including movement, sensation, thought, memory, and emotion. The brain receives information from neurons, interprets that information, and then responds via either voluntary or involuntary actions. When the brain is affected by disorders, such as epilepsy, seizures, migraines, and intracranial emergencies, the proper functioning of the body can be severely impaired (see Figure 12.2). This chapter will delve into these disorders, their impact on the brain, and common drugs used to treat these conditions.

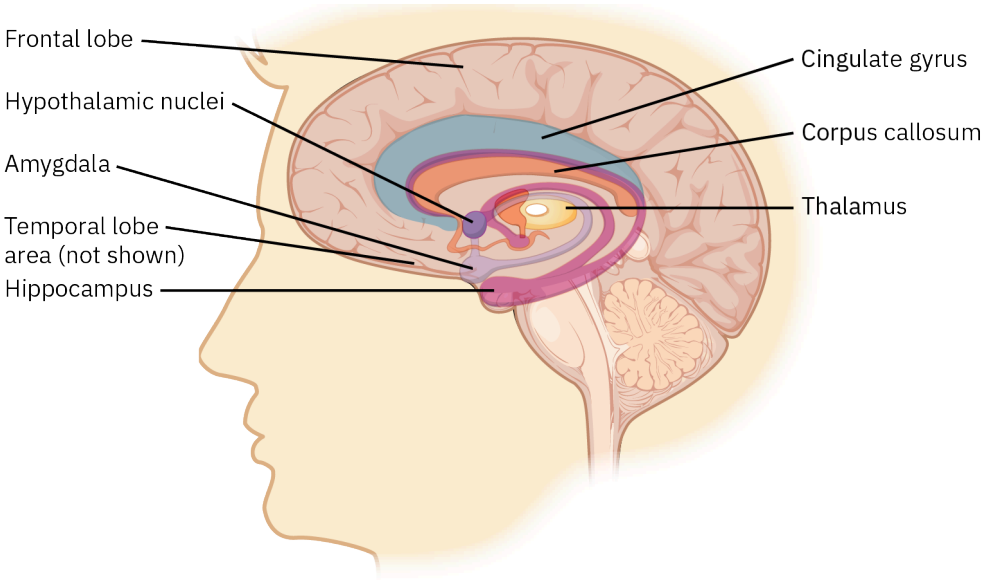


FIGURE 12.2 The hippocampus and amygdala, frontal lobe, and temporal lobe are common areas of the brain involved in seizures and epilepsy. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

12.1 Epilepsy and Anticonvulsant Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 12.1.1 Describe the pathophysiology of epilepsy.
- 12.1.2 Identify the clinical manifestations related to epilepsy.
- 12.1.3 Identify the etiology and diagnostic studies related to epilepsy.
- 12.1.4 Identify the characteristics of drugs used to treat epilepsy.
- 12.1.5 Explain the indications, action, adverse reactions, and interactions of drugs used to treat epilepsy.
- 12.1.6 Describe nursing implications of drugs used to treat epilepsy.
- 12.1.7 Explain the client education related to drugs used to treat epilepsy.

Overview of Epilepsy and Seizures

Seizures are a sudden and temporary disturbance in the electrical activity of the brain that can cause changes in behavior, movement, or consciousness. **Epilepsy**, on the other hand, is a neurological disorder characterized by recurrent seizures. In epilepsy, the seizures are typically unprovoked and can occur spontaneously without any apparent trigger. Epilepsy is a condition that affects approximately 3.4 million people in the United States, and it can have a significant impact on an individual's quality of life (Centers for Disease Control and Prevention, 2020a, 2020c).

Etiology

Seizures can have various causes such as fever, head injury, brain infection, drug or alcohol withdrawal or overdose, electrolyte imbalances, and metabolic disorders. Seizures may also result from brain tumors or masses, stroke, or other neurological conditions. Sometimes the cause of a seizure cannot be identified—a condition called an **idiopathic seizure** (Centers for Disease Control and Prevention, 2020b, 2020c).

Epilepsy, on the other hand, is a long-term neurological condition thought to be linked to abnormalities in the structure and function of the brain, which can be present at birth or develop later in life due to various factors such as brain injury, tumor, or stroke. Genetic factors may also play a role in the development of epilepsy. Understanding the underlying cause of epilepsy is important for effective diagnosis and treatment of the condition (Centers for Disease Control and Prevention, 2020a, 2020c).

Pathophysiology

A **seizure** occurs when there is a sudden and abnormal burst of electrical activity in the brain. This activity can

disrupt normal brain function and lead to a variety of symptoms, such as **convulsions**, loss of consciousness, and sensory or motor disturbances (Centers for Disease Control and Prevention, 2020a, 2020c).

Epilepsy is a chronic neurological disorder in which recurrent, unprovoked seizures occur. The underlying pathophysiology of epilepsy involves a disruption in the normal balance of excitatory and inhibitory activity in the brain. This imbalance can be due to structural or functional abnormalities in the brain, genetics, or changes in neurotransmitter activity. The abnormal electrical activity in the brain that occurs during an epileptic seizure is thought to be caused by a sudden release of excitatory neurotransmitters or a sudden decrease in inhibitory neurotransmitters (Centers for Disease Control and Prevention, 2020a, 2020c).

Diagnostic Testing

Diagnosis of seizures or epilepsy is multifaceted. The health care provider will obtain a thorough history and perform a neurological examination. The health care provider may order one or more of the following diagnostic tests to identify seizures or rule out other causes or structural abnormalities that could be contributing to the seizure diagnosis:

- **Electroencephalogram (EEG)**
  - An EEG is a test that measures changes in the brain's electrical patterns that relate to seizures or other neurological conditions. Small metal electrodes are attached to the scalp, and the electrical impulses of the brain appear as wavy lines on the EEG recording.
- **Computed tomography (CT) scan**
  - A CT scan is a noninvasive imaging procedure that uses x-rays to produce horizontal and axial images of the brain.
- **Magnetic resonance imaging (MRI)**
  - An MRI of the brain is a painless imaging procedure that uses large magnetic radio waves to produce clear images of the structures inside the skull.
- **Positron emission tomography (PET) scan**
  - A PET scan is an imaging procedure that uses a radioactive tracer substance to detect disease or injury in the brain.

Clinical Manifestations

Clinical manifestations of seizures can vary depending on the type of seizure a person is experiencing. There are several types of seizures, but they are generally classified into two groups: **generalized seizures** and **focal seizures**.

Generalized seizures involve abnormal activity in both sides of the brain from the beginning of the seizure. The two types of generalized seizures are **absence seizures** and **tonic-clonic seizures** (Centers for Disease Control and Prevention, 2020a, 2020c).

- Absence seizures, also known as **petit mal seizures**, cause rapid blinking or a few seconds of staring into space.
- Tonic-clonic seizures involve both tonic (muscle stiffness) and clonic (muscle jerking) phases and are commonly known as **grand mal seizures**.

Focal seizures, also known as **partial seizures**, begin in a specific area of the brain and can cause a wide range of symptoms depending on the area of the brain that is affected. There are three types of focal seizures: **simple focal seizures**, **complex focal seizures**, and **secondary generalized seizures** (Centers for Disease Control and Prevention, 2020a, 2020c).

- Simple focal seizures affect a small part of the brain and cause twitching movements or a change in sensation, such as an odd taste or smell.
- Complex focal seizures make a person confused or dazed. The person will be unresponsive to questions or directions for up to a few minutes.
- Secondary generalized seizures begin in one part of the brain but then spread to the other side. The person first has a focal seizure, followed by a generalized seizure.

LINK TO LEARNING

Epilepsy and Seizures

Access multimedia content (https://openstax.org/books/pharmacology/pages/12-1-epilepsy-and-anticonvulsant-drugs)
Alila Medical Media presents an educational video on epilepsy and seizures.

Drugs Used to Treat Epilepsy

Drugs that are used to treat epilepsy and seizures are generally termed **anticonvulsant drugs**. Anticonvulsant drugs are used to either control acute seizures or as maintenance to prevent seizures from occurring. Other drug classifications, such as some central nervous system depressants and mood stabilizers, have also been shown to be effective in the treatment of seizures and epilepsy. This section of the chapter will cover commonly prescribed classes of drugs used to treat seizures and epilepsy: hydantoins, barbiturates, succinates, benzodiazipines, iminostilbenes, valproates, pyrrolidine derivatives, and other anticonvulsants.

Importantly, numerous medications utilized for epilepsy treatment may interact with other drugs. Therefore, the nurse should thoroughly evaluate all the medications a client is currently taking, including over-the-counter products and herbal supplements. If any questions or concerns arise, the nurse should consult with a more knowledgeable health care provider or pharmacist to ensure the client's safety and prevent the occurrence of potential drug interactions.

Hydantoins

Hydantoins are a class of anticonvulsant drugs that are used to prevent or control seizures. Hydantoins can reduce the occurrence and severity of seizures by stabilizing the neuronal membrane in the brain. Some commonly prescribed hydantoins include phenytoin and fosphenytoin. Although hydantoins can be effective in controlling seizures, they can have significant adverse effects, including dizziness, drowsiness, and coordination problems. Long-term use can lead to complications such as osteoporosis and **gingival hyperplasia** (gum overgrowth). Contraindications of hydantoins include hypersensitivity to hydantoins or substances they contain, sinus bradycardia or heart block, and liver disease. They should be used cautiously in people who are pregnant or breastfeeding as they can be harmful to the fetus or infant (Gupta & Tripp, 2022).

Therapeutic drug monitoring, which may be necessary for optimal treatment outcomes, is an essential task for nurses. Careful review of serum blood levels—trough levels and peak levels—is crucial to make appropriate dosing adjustments. Trough levels indicate the lowest concentration of the drug in the blood and are typically measured just before the client's next scheduled dose. As a valuable indicator of the clinically effective range of serum levels, trough levels help confirm client compliance.

On the other hand, peak levels are indicative of an individual's threshold for potential dose-related adverse effects and are measured at the peak concentration time. The goal is to achieve a therapeutic effect without clinical signs of toxicity, which is more likely to occur when serum total concentrations range between 10 and 20 mcg/mL. Therefore, close monitoring of serum blood levels, including both trough and peak levels, enables health care providers to optimize dosing, maximize therapeutic benefits, and minimize the risk of adverse effects.

Phenytoin (Dilantin) is the most prescribed hydantoin. Table 12.1 is a drug prototype table for hydantoins featuring phenytoin. It lists drug class, mechanism of action, adult and pediatric dosages, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anticonvulsant **Mechanism of Action** Decreases abnormal electrical activity in the brain through a voltage-dependent blockade of membrane sodium channels that are responsible for action potential	**Drug Dosage** Individualized based on disease process. *Adults:* Initial dose: 100 mg extended-release capsule orally 3 times daily. Upward titration with a maximum of 2 capsules 3 times daily. Serum blood level determinations may be necessary for optimal dosing adjustments. *Children:* Initial dose: 5 mg/kg/day in 2 or 3 equally divided doses, with subsequent dosage individualized to a maximum of 300 mg daily. Recommended daily maintenance dosage: 4–8 mg/kg. Children >6 years old and adolescents may require the minimum adult dose (300 mg/day).
Indications To treat tonic-clonic and psychomotor seizures To prevent and treat seizures that occur during neurosurgery **Therapeutic Effects** Reduces seizure activity	**Drug Interactions** Azoles Antineoplastic agents Delavirdine Neuromuscular blocking agents Warfarin Calcium channel blockers Antilipemic agents Antacids **Food Interactions** No significant interactions
Adverse Effects Nystagmus Ataxia Slurred speech Decreased coordination Somnolence Mental confusion	**Contraindications** Hypersensitivity Prior history of acute hepatotoxicity attributed to phenytoin Bradycardia or heart block Caution: Monitor closely clients who have depression because this drug can increase suicidal thoughts or behavior Caution also advised for using this drug during pregnancy because it may cause potential harm to the fetus

TABLE 12.1 **Drug Prototype Table: Phenytoin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Barbiturates

Barbiturates are a class of drugs that act as central nervous system depressants, leading to sedation and relaxation. Barbiturates work by enhancing the actions of **Gamma-aminobutyric acid (GABA)**, the neurotransmitter that slows down brain activity. GABA is boosted by barbiturates, making them useful as sedatives, hypnotics, and anticonvulsants. Notably, barbiturates have a high risk of addiction, tolerance, and overdose, so their use has declined in favor of safer alternatives. Common adverse effects of barbiturates include dyspnea, confusion, bradycardia, dizziness, drowsiness, nausea, and vomiting. This class of drugs is contraindicated in people with hypersensitivity to barbiturates or their components, in those with hepatic insufficiency, and in those with respiratory disorders (Skibiski & Abdijadid, 2022).

Phenobarbital is the most used barbiturate for the treatment of seizures. Therapeutic drug monitoring is required. Phenobarbital is also a strong CYP inducer and will decrease the concentration of many other drugs. Table 12.2 is a drug prototype table for barbiturates featuring phenobarbital. It lists drug class, mechanism of action, adult and

pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Barbiturate **Mechanism of Action** Inhibits the central nervous system by enhancing GABA, which slows activity in the brain	**Drug Dosage** Individualized based on disease process. *Tablet:* *Adults:* 50–100 mg orally 2 to 3 times daily. Titrate based on response and therapeutic drug monitoring. *Children:* Loading dose of 15–20 mg/kg produces blood levels of about 20 mcg/mL shortly after administration. *Elixir:* *Adults*: 60–200 mg daily. *Children:* 3–6 mg/kg/day. *Intramuscular or intravenous (IV)* *Adults:* 20–320 mg repeated every 6 hours as necessary. *Children:* 4–6 mg/kg/day for 7–10 days to blood level of 10–15 mcg/mL or 10–15 mg/kg/day.
Indications To treat seizures As a sedative **Therapeutic Effects** Reduces seizures Enhances sleep	**Drug Interactions** Anticoagulants Corticosteroids Griseofulvin Doxycycline Phenytoin, sodium valproate, valproic acid Monoamine oxidase inhibitors (MAOIs) Estradiol, estrone, progesterone, and other steroidal hormones Other central nervous system depressants **Food Interactions** No significant interactions
Adverse Effects Central nervous system depression (drowsiness, lethargy, vertigo, drowsiness) Respiratory depression Nausea Vomiting Headache	**Contraindications** Hypersensitivity Hepatic failure Respiratory disease Caution: Monitor closely for drug addiction and dependence Caution also advised during pregnancy because drug may cause fetal malformations

TABLE 12.2 **Drug Prototype Table: Phenobarbital** (source: https://dailymed.nlm.nih.gov/dailymed/)

Succinates

Succinates are a class of drugs that are used to treat seizures, including petit mal seizures. Succinates reduce the amount of calcium available for nerve activity by blocking calcium channels in the brain; abnormal electrical activity in the brain is then reduced, which helps to decrease the occurrence of seizures. Adverse effects include gastrointestinal upset, drowsiness, lethargy, hiccups, and headaches. They are contraindicated in persons with hypersensitivity to succinates or their properties and should be used cautiously in clients with renal or hepatic insufficiency (Hanrahan & Carson, 2022).

Ethosuximide (Zarontin) is the most used succinate. Table 12.3 is a drug prototype table for succinates featuring ethosuximide. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anticonvulsant **Mechanism of Action** Blocks calcium channels in the brain, reducing the amount of calcium available for neuronal activity	**Drug Dosage** Individualized based on disease process. *Adults:* 500 mg orally daily (typically in 2 divided doses). Upward titration by 250 mg every 4–7 days to keep plasma ranges of 40–100 mcg/mL. *Children:* The *initial* oral dose for clients 3–6 years of age is 1 capsule (250 mg) daily; for clients ≥6 years of age, 2 capsules (500 mg) daily.
Indications To treat seizures **Therapeutic Effects** Reduces seizures	**Drug Interactions** Phenytoin Valproic acid **Food Interactions** No significant interactions
Adverse Effects Gastrointestinal upset (anorexia, nausea/vomiting, diarrhea, abdominal pain) Leukopenia Drowsiness Headache Dizziness Hiccups Pruritus/rash	**Contraindications** Hypersensitivity Caution: Use cautiously in people who are taking other anticonvulsant drugs as it may increase their serum levels Caution also advised during pregnancy as this drug may cause fetal malformations

TABLE 12.3 **Drug Prototype Table: Ethosuximide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Benzodiazepines

Benzodiazepines are a class of drug that act on the benzodiazepine receptors (BZ-Rs) in the central nervous system. They work by enhancing the activity of the neurotransmitter GABA, which is inhibitory and slows brain activity. Dosing is individualized and depends on the drug being used. Benzodiazepines such as clonazepam, clorazepate, and diazepam are commonly prescribed to treat seizures.

Nurses should note that these drugs can result in sedation and use of these drugs in late pregnancy can result in sedation (respiratory depression, lethargy, hypotonia) and/or withdrawal symptoms (hyperreflexia, irritability, restlessness, tremors, inconsolable crying, and feeding difficulties) in newborns.

Table 12.4 lists common benzodiazepines and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Clonazepam (Klonopin)	*Adults:* Initial dose: 1.5 mg/day orally divided into 3 doses. Increase dose by 0.5–1 mg every 3 days until seizures are adequately controlled. *Children (up to 10 years of age or 30 kg of body weight)*: Initial dose: 0.01–0.03 mg/kg/day; do not exceed 0.05 mg/kg/day given in 2 or 3 divided doses. Dosage should be increased by no more than 0.25–0.5 mg every third day until a daily maintenance dose of 0.1–0.2 mg/kg of body weight has been reached and seizures are controlled. Whenever possible, the daily dose should be divided into 3 equal doses. If this is not feasible, give the largest dose before bedtime.

TABLE 12.4 **Drug Emphasis Table: Benzodiazepines** (source: https://dailymed.nlm.nih.gov/dailymed/)

Clorazepate	*Adults:* The maximum recommended initial dose in clients over 12 years old is 7.5 mg 3 times daily. Increase dose by no more than 7.5 mg every week to a maximum of 90 mg/day. *Children (9–12 years):* The maximum recommended initial dose is 7.5 mg 2 times a daily. Increase dose by no more than 7.5 mg every week not to exceed 60 mg/day.
Diazepam (Valium, Diastat, Valtoco)	*Adults:* 5–10 mg IV slowly; if seizure continues or recurs, may repeat if necessary at 10- to 15-minute intervals up to a maximum dose of 30 mg. *Children (3 months to 17 years of age with status epilepticus):* *First dose:* 0.2 mg/kg (maximum 8 mg) by slow intravenous push (1 minute in duration). *Second dose:* (If necessary; 5 minutes after the first dose): 0.1 mg/kg (maximum 4 mg) by slow intravenous push (1 minute in duration). *Adults:* 2–10 mg orally 2–4 times daily. *Children:* 1–2.5 mg, 3 or 4 times daily orally initially; increase gradually as needed and tolerated. Because of varied responses to central nervous system–acting drugs, initiate therapy with lowest dose and increase as required. Not for use in children under 6 months.
Lorazepam (Ativan)	Individualized based on disease process. *Adults:* Oral dosing of 2–6 mg/day given in divided doses 2 to 3 times daily. IV dosing of 4 mg given slowly. If seizure continues or recurs after 10- to 15-minute observation period, an additional 4 mg IV may be slowly administered. *Children:* Not recommended in children less than 18 years of age.

TABLE 12.4 Drug Emphasis Table: Benzodiazepines (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects of benzodiazepines include respiratory depression, drowsiness, confusion, headache, dizziness, tremor, and gastrointestinal upset. Benzodiazepines are contraindicated in hypersensitivity to the drug and its properties, in angle closure glaucoma, and with concomitant use with opioids. An increased risk of congenital malformations and other developmental abnormalities associated with benzodiazepine use during pregnancy has been identified.

Seizure rescue with benzodiazepines is a commonly used approach to manage seizures quickly and effectively. Benzodiazepines suppress excessive electrical activity in the brain. When a seizure occurs, administering a benzodiazepine promptly can help terminate the seizure and prevent its progression These medications can be administered orally, intravenously, intramuscularly, and via other routes depending on the situation and available resources.

The goal of seizure rescue with benzodiazepines is to provide rapid and effective control of seizures while ensuring the safety and well-being of the client. Benzodiazepines are a short-term solution for seizure management. Long-term treatment plans and adjustments should be made in collaboration with a health care provider to address the underlying cause of the seizure and prevent future occurrences.

Another widely used benzodiazepine for treating seizures is lorazepam. Table 12.5 is a drug prototype table for benzodiazepines featuring lorazepam. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Benzodiazepine **Mechanism of Action** Binds to the benzodiazepine receptors on the postsynaptic GABA-A ligand-gated chloride channel neuron in the central nervous system, thereby enhancing the inhibitory effects of GABA	**Drug Dosage** Individualized based on disease process. *Adults:* Oral dosing of 2–6 mg/day given in divided doses 2 to 3 times daily. IV dosing of 4 mg given slowly. If seizure continues or recurs after 10- to 15-minute observation period, an additional 4 mg IV may be slowly administered. *Children:* Not recommended in children less than 18 years of age.
Indications To treat seizures Preanesthetic **Therapeutic Effects** Reduces seizures Sedation	**Drug Interactions** Opioids Scopolamine Probenecid **Food Interactions** No significant interactions
Adverse Effects Hypotension Confusion Somnolence Headache Leukocytosis Respiratory suppression	**Contraindications** Hypersensitivity Acute narrow angle glaucoma Respiratory insufficiency Pregnancy/breastfeeding Caution: Use cautiously with other drugs that suppress the central nervous system due to respiratory suppression

TABLE 12.5 **Drug Prototype Table: Lorazepam** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Benzodiazepines

Benzodiazepines—when used in combination with opioid drugs—may depress the central nervous system, causing serious adverse effects including respiratory depression and death.

CLINICAL TIP

Lorazepam Intravenous Administration

Intravenous administration of lorazepam should be via slow intravenous push (2 mg/minute) for active seizures. If respiratory depression develops, flumazenil should be used as a competitive antagonist to reverse the effects of the lorazepam (Ghiasi et al., 2023).

SPECIAL CONSIDERATIONS

Substance Misuse and Dependence

Barbiturates and benzodiazepines are highly addictive and can result in dependence, tolerance, and even overdose. It is important for the health care provider to consider the client's situation and perform a thorough medical and social history, including substance misuse or problematic use, which may also be referred to as substance abuse.

- *Drug tolerance* occurs when someone uses, misuses, or overuses a substance over a long period of time.

- *Dependence* occurs when someone uses high doses of a substance and they cannot function normally without the use of the substance.
- *Substance use disorder* occurs when someone is unable to control the use of the substance and they cannot stop using the substance.
- *Overdose* occurs when someone takes in a toxic amount of a substance. Overdose can lead to coma or even death.

(Source: Jahan & Burgess, 2022)

The National Institute on Drug Abuse (NIDA) (https://openstax.org/r/nidanih) is the leading federal agency supporting scientific research on substance use disorders. The NIDA provides research, education, and training resources and plays a role in the National Institute of Health HEAL (Helping to End Addiction Long-Term) Program (https://openstax.org/r/healnih), which looks at substance use disorders as a public health emergency in the United States.

The Substance Abuse and Mental Health Services Administration (SAMHSA) (https://openstax.org/r/samhsa) is a national helpline and confidential treatment referral service that provides clients and their families with needed resources regarding substance use disorders and mental health issues.

Iminostilbenes

Iminostilbenes are a class of anticonvulsant drug in which the compounds are structurally related to cyclic antidepressants. This class of drug shows efficacy in the first-line treatment for seizures. Iminostilbenes inhibit neuronal excitability by enhancing GABA; this drug requires therapeutic monitoring. Adverse reactions include urticaria, photosensitivity, congestive heart failure, edema, dyspnea, acute urinary retention, drowsiness, dizziness, coordination disturbances, headache, fatigue, abdominal pain, agranulocytosis, hyponatremia/SIADH, and leukopenia. Iminostilbenes are contraindicated in individuals with previous bone marrow depression and with hypersensitivity to the drug or its constituents; they should not be administered with tricyclic antidepressants, monoamine oxidase (MAO) inhibitors, nefazodone, and delavirdine (Magheru et al., 2022).

The most common iminostilbene used in the treatment of seizures is carbamazepine (Tegretol). Table 12.6 is a drug prototype table for iminostilbenes featuring carbamazepine. It lists drug class, mechanism of action, adult and pediatric dosages, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anticonvulsant **Mechanism of Action** Inhibits neuronal excitability by enhancing GABA, which decreases brain activity	**Drug Dosage** Individualized based on disease process and serum blood levels. *Adults and children over 12 years of age:* Initial dose of 200 mg orally twice daily. Increase at weekly intervals by adding up to 200 mg/day until the optimal response is obtained. Maintenance dosage to the minimum effective level, usually 800–1200 mg daily. Extended release: Initial dose of 200 mg orally twice daily. Increase weekly by adding 200 mg/day using a twice daily regimen until optimal response is reached. Maximum dose: 800–1200 mg daily. *Children 6–12 years of age:* Initial dose of 100 mg twice daily for tablets (200 mg/day). Increase at weekly intervals by adding up to 100 mg/day using a 3–4 times daily regimen of carbamazepine tablets until the optimal response is obtained. Dosage generally should not exceed 1000 mg daily. *Maintenance:* Adjust dosage to the minimum effective level, usually 400–800 mg daily. *Children <6 years of age:* Initial dose of 10–20 mg/kg twice daily or 3 times daily as tablets. Increase weekly to achieve optimal clinical response administered 3 or 4 times daily. *Maintenance:* Typically, optimal clinical response is achieved at daily doses below 35 mg/kg. If satisfactory clinical response not achieved, measure plasma levels to determine if they are in the therapeutic range. No recommendation regarding safety of carbamazepine for use at doses above 35 mg/kg/24 hours.
Indications To treat seizures **Therapeutic Effects** Reduces seizure activity Sedation	**Drug Interactions** No significant drug interactions, other than contraindications listed below **Food Interactions** No significant interactions

TABLE 12.6 **Drug Prototype Table: Carbamazepine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects	Contraindications
Photosensitivity	Hypersensitivity
Edema	Bone marrow suppression
Dyspnea	Tricyclic antidepressants
Urinary retention	MAO inhibitors
Drowsiness	Nefazodone
Coordination disturbances	Delavirdine
Headache	
Fatigue	Caution:
Agranulocytosis	Monitor closely for serious dermatologic reactions including toxic epidermal necrolysis and Stevens-Johnson syndrome
Leukopenia	
Bone marrow depression	Monitor closely for hyponatremia and SIADH

TABLE 12.6 **Drug Prototype Table: Carbamazepine** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Carbamazepine

Carbamazepine may cause serious adverse effects including aplastic anemia and agranulocytosis.

Carbamazepine may cause serious dermatologic reactions including toxic epidermal necrolysis and Stevens-Johnson syndrome.

Valproates

Valproates are anticonvulsants and mood stabilizers used in the treatment of seizures and bipolar disorder. Valproates act on GABA levels in the central nervous system, blocking voltage-gated sodium, potassium, and calcium ion channels causing decreasing brain activity. Adverse reactions include headache, somnolence, dizziness, drowsiness, thrombocytopenia, tremor, alopecia, emotional lability, petechiae, rash, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevation, tinnitus, and photosensitivity. Valproates are contraindicated in individuals with hepatic disorders and in those who have hypersensitivity to components of the drug.

Therapeutic drug monitoring measures the concentration of a valproic acid in the client's blood and ensures that the drug is within the therapeutic range by adjusting the dosage, if necessary. Therapeutic range for valproic acid varies depending on the indication being treated. Generally, the total serum concentration of valproic acid is maintained between 50 and 100 µg/mL for epilepsy. However, individualized target ranges may be established based on factors such as age, comorbidities, concomitant medications, and treatment responses.

The most common valproate is valproic acid (Rahman & Nguyen, 2022). Table 12.7 is a drug prototype table for valproates featuring valproic acid. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anticonvulsant and mood stabilizer **Mechanism of Action** Acts on the GABA levels in the central nervous system: blocking voltage-gated sodium, potassium, and calcium ion channels and decreasing brain activity	**Drug Dosage** Individualized based on disease process. *Adults and children ≥10 years:* 15 mg/kg/day. Increase at 1-week intervals by 5–10 mg/kg/day until seizures are controlled or side effects preclude further increases. *Maximum recommended dosage:* 60 mg/kg/day. If total daily dose exceeds 250 mg, it should be given in divided doses. Therapeutic drug monitoring range between 50–100 µg/mL.
Indications To treat seizures To treat bipolar disorder **Therapeutic Effects** Reduces seizure activity Reduces bipolar symptoms of mania	**Drug Interactions** Amitriptyline/nortriptyline Carbamazepine Clonazepam Diazepam Ethosuximide Lamotrigine Phenobarbital Phenytoin Propofol Rufinamide Tolbutamide Warfarin Zidovudine **Food Interactions** No significant interactions
Adverse Effects Headache Somnolence Dizziness Drowsiness Thrombocytopenia Emotional lability Rash Elevated liver enzymes Tinnitus	**Contraindications** Hypersensitivity Hepatic insufficiency Bone marrow depression Pregnancy Caution: Monitor closely for suicidal behavior and ideation Should be stopped if client develops acute pancreatitis

TABLE 12.7 **Drug Prototype: Valproic Acid** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Valproates

Valproates may cause serious adverse effects including pancreatitis, abnormal bleeding, and clotting times. Valproates are known to cause abnormalities in the development of the fetus.

Pyrrolidine Derivatives

Pyrrolidine derivatives are novel anticonvulsant drugs used to treat seizures that were FDA approved in 2000. Pyrrolidine derivatives come in IV and oral formularies. Adverse effects include abdominal pain, nausea, anorexia, leukopenia, headache, mood swings, fatigue, somnolence, confusion, and increased risk for suicide. They are contraindicated with hypersensitivity to any of the drug's components and in individuals with renal impairment.

Levetiracetam (Keppra) is the most used pyrrolidine derivative. Table 12.8 is a drug prototype table for pyrrolidine derivatives featuring levetiracetam. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class
Pyrrolidines

Mechanism of Action
Binds to a unique synaptic vesicle protein 2A (SV2A)—SV2A protein is a part of secretory vesicle membranes that mediates calcium-dependent vesicular neurotransmitter release; the binding of levetiracetam to SV2A appears to decrease the rate of vesicle release

Drug Dosage
Individualized based on disease process.
Adults and adolescents ≥16 years of age: Initiate treatment with a daily dose of 1000 mg/day, given as twice-daily dosing (500 mg twice daily).
Additional dosing increments may be given (1000 mg/day additional every 2 weeks) to a maximum recommended daily dose of 3000 mg.
Children <16 years of age:
1 month to <6 months: Initiate treatment with a daily dose of 14 mg/kg in 2 divided doses (7 mg/kg twice daily). Increase the daily dose every 2 weeks by increments of 14 mg/kg to the recommended daily dose of 42 mg/kg (21 mg/kg twice daily). In the clinical trial, the mean daily dose was 35 mg/kg in this age group.
6 months to <4 years: Initiate treatment with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). Increase the daily dose in 2 weeks by an increment of 20 mg/kg to the recommended daily dose of 50 mg/kg (25 mg/kg twice daily). If a client cannot tolerate a daily dose of 50 mg/kg, the daily dose may be reduced. In the clinical trial, the mean daily dose was 47 mg/kg in this age group.
4 years to <16 years: Initiate treatment with a daily dose of 20 mg/kg in 2 divided doses (10 mg/kg twice daily). Increase the daily dose every 2 weeks by increments of 20 mg/kg to the recommended daily dose of 60 mg/kg (30 mg/kg twice daily). If a client cannot tolerate a daily dose of 60 mg/kg, the daily dose may be reduced. In the clinical trial, the mean daily dose was 44 mg/kg.
Maximum dose: 3000 mg/day.

Indications
To treat seizures

Therapeutic Effects
Reduces seizures
Sedation

Drug Interactions
Baclofen
Melatonin
Opioids
Trazodone

Food Interactions
No significant interactions

Adverse Effects
Somnolence
Fatigue
Rash
Coordination difficulties
Emotional lability
Headache

Contraindications
Hypersensitivity

Caution:
Monitor closely for behavioral abnormalities such as increase in aggression, agitation, or anger and for psychotic symptoms such as hallucinations and delirium

TABLE 12.8 **Drug Prototype Table: Levetiracetam** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Levetiracetam

Levetiracetam may cause serious or life-threatening behavioral manifestations and psychotic symptoms, including aggression, hostility, and homicidal ideation.

Other Anticonvulsants

There are many other anticonvulsants on the market; novel drugs continue to appear as treatment options improve. Table 12.9 lists common anticonvulsant drugs and typical routes and dosing for adult and pediatric clients.

Drug	Class and Indication	Mechanism of Action	Adverse Effects and Contraindications	Dosage and Routes of Administration
Gabapentin (Neurontin)	Anticonvulsant *Indication:* Adjunctive therapy for partial onset seizures, with or without secondary generalization, in adults and children 3 years and older with epilepsy	Increases the concentration and probably the rate of synthesis of GABA in brain, which may enhance non-vesicular GABA release during seizures	*Adverse Effects:* in clients >12 years of age: Somnolence, dizziness, ataxia, fatigue, and nystagmus *In clients 3–12 years:* Viral infection, fever, nausea and/or vomiting, somnolence, and hostility *Contraindications:* Hypersensitivity to the drug or its ingredients	*In clients ≥12 years of age:* Starting dose: 300 mg orally 3 times daily. Recommended maintenance is 300–600 mg 3 times daily. *In clients 3–11 years:* Starting dose range is 10–15 mg/kg/day orally given in 3 divided doses and the recommended maintenance dose reached by upward titration over a period of 3 days. *Recommended maintenance dose for 3–4 years of age:* 40 mg/kg/day orally in 3 divided doses. *Recommended maintenance dose for 5–11 years of age:* 25–35 mg/kg/day orally in 3 divided doses.
Lamotrigine (Lamictal)	Anticonvulsant *Indication:* Adjunctive therapy for partial seizures	Blocks voltage-gated sodium ion channels and inhibits presynaptic glutamate and aspartate release	*Adverse Effects:* GI upset, dizziness, drowsiness, blurred vision, fatigue, and rash related to Stevens-Johnson syndrome *Contraindications:* Hypersensitivity to the drug or its ingredients	*Oral dosing (in clients taking Valproate concurrently):* *Weeks 1 and 2:* 25 mg every other day. *Weeks 3 and 4:* 25 mg daily. *Week 5 onward*: Increase by 25–50 mg/day every 1–2 weeks. *Maintenance dose:* 200–250 mg daily. *Extended-release oral dosing (in clients taking Valproate concurrently):* *Weeks 1 and 2:* 25 mg every other day. *Weeks 3 and 4:* 25 mg daily. *Week 5:* 50 mg daily. *Week 6:* 100 mg daily. *Week 7:* 150 mg daily. *Maintenance dose:* 200–250 mg daily. Maximum dose: 400 mg/day

TABLE 12.9 **Drug Emphasis Table: Other Anticonvulsants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Class and Indication	Mechanism of Action	Adverse Effects and Contraindications	Dosage and Routes of Administration
Topiramate (Topamax, Qudexy, Trokendi)	Anticonvulsant, Other *Indication:* Treatment of partial or generalized seizures	Stimulates GABA-A receptor activity at brain non-benzodiazepine receptor sites and reduces glutamate activity	*Adverse Effects:* Drowsiness, somnolence, fatigue, coordination difficulties *Contraindications:* Hypersensitivity to the drug or its ingredients	*Adults and children ≥10 years of age:* 400 mg/day orally in 2 divided doses. The dose should be achieved by titrating as follows: *Week 1:* 25 mg in morning and evening. *Week 2:* 50 mg in morning and evening. *Week 3:* 75 mg in morning and evening. *Week 4:* 100 mg in morning and evening. *Week 5:* 150 mg in morning and evening. *Week 6:* 200 mg in morning and evening. *Maximum dose:* 400 mg/day. *Children 2–9 years of age:* Dosing in clients 2–9 years of age based on weight. Initial dose: 25 mg/day nightly for the first week. The dosage can be increased to 50 mg/day (25 mg twice daily) in the second week. During subsequent weeks, the dosage can be increased by 25–50 mg/day as tolerated. Titration to the minimum maintenance dose should be attempted over 5–7 weeks of the total titration period. Additional titration to a higher dose (up to the maximum maintenance dose) can be attempted at 25–50 mg/day weekly increments.

TABLE 12.9 **Drug Emphasis Table: Other Anticonvulsants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Class and Indication	Mechanism of Action	Adverse Effects and Contraindications	Dosage and Routes of Administration
Lacosamide (Vimpat, Motpoly XR)	Anticonvulsant, Other *Indication:* Treatment of partial seizures	Blocks voltage-gated sodium ion channels and decreases brain activity	*Adverse Effects:* Dizziness, nausea, headache, fatigue, drowsiness *Contraindications:* Hypersensitivity, second- and third-degree atrioventricular (AV) block, which may cause severe bradycardia	*Adults and adolescents ≥17 years of age or older:* Initial dose: 100 mg orally twice daily or 200 mg single loading dose, followed 12 hours later by 100 mg twice daily. Increase by 50 mg twice daily every week to reach maintenance dose of 150–200 mg twice daily. *Children weighing >50 kg:* Initial dose 50 mg orally twice daily or 100 mg daily. Increase by 50 mg twice daily or 100 mg daily every week. *Maintenance dose:* 150–200 mg twice daily or 300–400 mg daily. *Children weighing 30–50 kg:* Initial dose: 1 mg/kg orally twice daily or 2 mg/kg daily. Increase by 1 mg/kg twice daily or 2 mg/kg daily every week. *Maintenance:* 2 mg/kg twice daily or 4–8 mg/kg/day. *Children weighing 11–<30 kg:* Initial dose: 1 mg/kg orally twice daily or 2 mg/kg daily. Increase by 1 mg/kg twice daily or 2 mg/kg daily every week. *Maintenance:* 3–6 mg/kg twice daily or 6–12 mg/kg/day.
Zonisamide (Zonegran, Zonisade)	Sulfonamide anticonvulsant *Indication:* Adjunctive therapy for partial seizures	Blocks voltage-gated sodium ion channels and inhibits presynaptic glutamate and aspartate release	*Adverse Effects:* Headache, fatigue, coordination difficulties, visual disturbances, drowsiness *Contraindications:* Hypersensitivity to the drug or its ingredients	*Adults and adolescents ≥16 years of age:* Initial dose: 100 mg orally daily. After 2 weeks the dose may be increased to 200 mg/day for at least 2 weeks. It can be increased to 300 mg/day and 400 mg/day with at least 2 weeks at each dose to achieve steady state at each level.

TABLE 12.9 **Drug Emphasis Table: Other Anticonvulsants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking anticonvulsant drugs:

- Assess the client's medical history, current drug list, and allergies.
- Assess client's baseline weight and vital signs.
- Ensure the drug is prepared appropriately using aseptic technique and verify dosage before administration.
- Monitor the client's response to the drug, including any changes in seizure patterns, neurological condition, and mental status.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an anticonvulsant drug should:

- Take the drug as prescribed and do not skip doses or stop therapy.
- Do not use alcohol or smoke—alcohol can depress the central nervous system, and smoking may cause vasoconstriction, resulting in reduced elimination of the drug.
- Keep a journal of symptoms and note improved or worsening symptoms.
- Take drug with food if gastrointestinal upset occurs.
- Have laboratory testing as scheduled by health care provider. Many anticonvulsants require titration and monitoring of blood levels to ensure safety and efficacy.
- Report symptoms of dyspnea, confusion, skin rash, abnormal bleeding, and/or infections to health care provider as these may represent an adverse reaction to anticonvulsant drugs.
- Speak to their health care provider if they are pregnant or plan to become pregnant before starting these drugs because they can impact the fetus.
- Store out of reach children and away from heat, moisture, and light.

The client taking anticonvulsant drugs *should not*:

- Drive or operate machinery with central nervous system depressants.
- Stop taking the drug unless directed by their health care provider, as this drug class reduces the risk of seizures.

FDA BLACK BOX WARNING

Lamotrigine

Lamotrigine may cause serious dermatologic reactions such as Stevens-Johnson syndrome or toxic epidermal necrosis.

12.2 Migraine Headaches and Migraine Headache Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 12.2.1 Describe the pathophysiology of migraine headaches.
- 12.2.2 Identify the clinical manifestations related to migraine headaches.
- 12.2.3 Identify the etiology and diagnostic studies related to migraine headaches.
- 12.2.4 Identify the characteristics of drugs used to treat migraine headaches.
- 12.2.5 Explain the indications, action, adverse reactions, and interactions of drugs used to treat migraine headaches.
- 12.2.6 Describe nursing implications of drugs used to treat migraine headaches.
- 12.2.7 Explain the client education related to drug used to treat migraine headaches.

Headaches are a prevalent medical condition that can cause pain or discomfort in the head or neck area. Among the

different types of headaches, **migraine headaches** are a specific and recurring type of headache that can cause significant debilitating symptoms. This chapter will focus specifically on migraine headaches, exploring their causes, symptoms, and common drugs used to alleviate this condition.

Overview of Migraine Headaches

Migraine headaches are a type of headache that can be recurring and are often associated with a range of symptoms that can greatly affect a person's quality of life. These symptoms will be explored in more detail later in this chapter. Migraine headaches can last for several hours up to several days and can be debilitating, often interfering with daily activities. Some people may experience a warning symptom, known as an **aura**, which can include visual disturbances such as flashing lights or blind spots. Migraine headaches are a prevalent condition that affects a significant portion of the U.S. population, with an estimated 39 million people experiencing this type of headache (American Migraine Foundation, 2023).

Etiology

Migraines can stem from a range of factors, which may include environmental, potent odors, tobacco use, motion sickness, hormonal fluctuations, flashing lights, inadequate sleep, heightened stress levels, and certain foods such as aged cheeses, aspartame, and monosodium glutamate (MSG), and caffeine withdrawal (American Migraine Foundation, 2023; National Institute of Neurological Disorders and Stroke, 2023).

Pathophysiology

The underlying pathophysiology of migraine headaches is unclear, but a comprehensive theory proposes the involvement of neuronal hyperexcitability, vasodilation of blood vessels—which triggers pain receptors—and inflammation in the brain (American Migraine Foundation, 2023).

Diagnostic Testing

To diagnose migraine headaches, health care providers rely on the client's report of symptoms, a detailed medical history, and a physical examination. Radiologic imaging, such as an MRI or CT scan, may also be performed to rule out other potential causes of the headaches, such as brain tumors, meningitis, or ischemia (American Migraine Foundation, 2023).

Clinical Manifestations

Clinical manifestations (symptoms) of migraine headaches include:

- Pulsating, throbbing head pain
- Muscle weakness
- Language disturbances
- Pupillary changes
- Visual disturbances
- Mood changes
- Fluid retention
- Increased urinary output

LINK TO LEARNING

What Is Migraine Disease?

Access multimedia content (https://openstax.org/books/pharmacology/pages/12-2-migraine-headaches-and-migraine-headache-drugs)

Nucleus Medical Media presents an educational video on migraine headaches.

Drugs Used to Treat Migraine Headaches

Migraine headaches can be treated through two distinct courses of therapy: abortive and preventive. **Abortive therapy** aims to relieve the symptoms of a migraine headache through drug administration. On the other hand, **preventive therapy** involves the use of drugs to prevent the occurrence of migraine headaches altogether.

Triptans

Triptans are **serotonin agonists** that target the pathophysiological mechanism of migraine headaches, effectively eliminating symptoms. By selectively binding to serotonin receptors 5-HT_{1B} and 5-HT_{1D}, triptans induce vasoconstriction of cranial arteries that are typically dilated during migraines. The vasoconstriction helps to reduce the intensity and duration of migraine headaches.

Table 12.10 lists common triptans and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Eletriptan (Relpax)	Single doses of 20–40 mg orally once. If the migraine does not resolve within 2 hours or returns after transient improvement, a second dose may be administered at least 2 hours after the first dose. Maximum daily dose should not exceed 80 mg.
Rizatriptan (Maxalt)	The recommended starting dose is either 5 mg or 10 mg orally once, for acute treatment of migraines in adults. May repeat dose after at least 2 hours if headache returns. Maximum daily dose should not exceed 30 mg.
Sumatriptan (Imitrex)	The recommended daily doses are 25 mg, 50 mg, or 100 mg orally. If the migraine has not resolved by 2 hours after taking sumatriptan or returns after a transient improvement, a second dose may be administered at least 2 hours after the first dose. Maximum daily dose is 200 mg in 24 hours. Subcutaneous dosing: 6 mg with a maximum dose of 12 mg/day. Maximum dosing should be 2–6 mg injections separated at least 1 hour apart. Intranasal doses: 5 mg, 10 mg, and 20 mg given as a single spray in one nostril. The maximum daily dose is 40 mg in a 24-hour period.
Zolmitriptan (Zomig)	The recommended starting dose is 1.25 mg or 2.5 mg. The maximum recommended single dose is 5 mg. If the migraine has not resolved by 2 hours after taking zolmitriptan or returns after a transient improvement, a second dose may be administered at least 2 hours after the first dose. Maximum daily dose is 10 mg in a 24-hour period.

TABLE 12.10 Drug Emphasis Table: Triptans (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of triptans include dizziness, nausea, flushing, tingling, neck pain, chest tightness, and paresthesia. Triptans are contraindicated in clients with a history of myocardial infarction, coronary artery disease, stroke, uncontrolled hypertension, and peripheral vascular disease (Nicholas & Nicholas, 2023).

Table 12.11 is a drug prototype table for triptans featuring sumatriptan. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Serotonin agonists **Mechanism of Action** Selectively binds to serotonin receptors 5-HT_{1B} and 5-HT_{1D} and induces vasoconstriction of cranial arteries	**Drug Dosage** The recommended daily doses are 25 mg, 50 mg, or 100 mg orally. If the migraine has not resolved by 2 hours after taking sumatriptan or returns after a transient improvement, a second dose may be administered at least 2 hours after the first dose. Maximum daily dose is 200 mg in 24 hours. Subcutaneous dosing: 6 mg with a maximum dose of 12 mg/day. Maximum dosing should be 2–6 mg injections separated at least 1 hour apart. Intranasal doses: 5 mg, 10 mg, and 20 mg given as a single spray in one nostril. The maximum daily dose is 40 mg in a 24-hour period.
Indications To treat migraine headaches To treat cluster headaches **Therapeutic Effects** Reduces migraine and cluster headaches	**Drug Interactions** Ergot-containing drugs Monoamine oxidase inhibitors Selective serotonin reuptake inhibitors Serotonin and norepinephrine reuptake inhibitors Tricyclic antidepressants **Food Interactions** No significant interactions
Adverse Effects Paresthesia Flushing Vertigo Malaise Hypotension Dystonia	**Contraindications** Hypersensitivity Ischemic coronary disease Stroke Peripheral vascular disease Uncontrolled hypertension Pregnancy Caution: Monitor closely for arrhythmias including ventricular tachycardia and ventricular fibrillation, which can lead to death

TABLE 12.11 **Drug Prototype Table: Sumatriptan** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Sumatriptan

There is cardiovascular risk from sumatriptan with an increased risk of adverse thrombotic events, including myocardial infarction and stroke.

Ergot Alkaloids

Ergot alkaloids are **alpha-adrenergic blockers**, a class of drug that directly stimulates vascular smooth muscle, thereby causing vasoconstriction. These alpha-adrenergic blockers are used in the treatment of migraine and vascular headaches as well as other medical conditions such as hypertension. Adverse effects include coronary and peripheral ischemia, muscle pains, nausea, vomiting, paresthesias, vertigo, weakness, and itching. Ergot alkaloids are contraindicated in hypersensitivity to the drug or any of its components, peripheral vascular disease, coronary heart disease, hypertension, impaired hepatic or renal function, and sepsis.

The most common ergot alkaloid used in the treatment of migraine headaches is ergotamine tartrate (Cafergot).

Table 12.12 is a drug prototype table for ergot alkaloids featuring ergotamine tartrate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Ergot alkaloid and alpha-adrenergic blocker **Mechanism of Action** Inhibits norepinephrine and directly stimulates vascular smooth muscle, causing vasoconstriction	**Drug Dosage** Starting dose: 1–2 mg sublingually at the first sign of a migraine and 1 mg additional sublingually every ½ hour, if needed for full relief. Maximum dose: 6 mg in 24 hours. Also available in suppository form and in tablets with caffeine.
Indications To treat migraine and vascular headaches **Therapeutic Effects** Reduces headache symptoms	**Drug Interactions** Ritonavir Indinavir Erythromycin Clarithromycin Troleandomycin **Food Interactions** No significant interactions
Adverse Effects Paresthesia Nausea Vomiting Weakness Vertigo Transient tachycardia or bradycardia Hypertension	**Contraindications** Hypersensitivity Vasoconstrictive conditions such as peripheral vascular disease and coronary heart disease Renal insufficiency Hepatic insufficiency Myocardial ischemia/infarction Caution: Monitor closely in clients who have bronchial asthma

TABLE 12.12 **Drug Prototype Table: Ergotamine Tartrate** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Ergotamine

Ergotamine is contraindicated with potent inhibitors CYP3A4 drugs. Concomitant use of these drugs may result in serious vasospasm producing cerebral limb ischemia.

Selective Serotonin Receptor Agonists

Selective serotonin receptor agonists are a novel drug class that is used in the treatment of migraine headaches. It is scentrally and peripherally acting 5-HT1F receptor agonist that decreases the release of neuropeptides and the neurotransmitter glutamate, thereby inhibiting neuronal firing. Adverse effects include paresthesia, fatigue, drowsiness, nausea, vomiting, muscle weakness, and hypertension. They are contraindicated in hypersensitivity to the drug or its components (Berger et al., 2020).

The most prescribed selective serotonin receptor agonist for migraine headaches is lasmiditan (Reyvow). Table 12.13 is a drug prototype table for selective serotonin receptor agonists featuring lasmiditan. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Selective serotonin receptor agonist **Mechanism of Action** Decreases the release of neuropeptides and the neurotransmitter glutamate, inhibiting neuronal firing	**Drug Dosage** Recommended dose is 50–200 mg taken orally, as needed. No more than 1 dose should be taken in 24 hours.
Indications To treat migraine and cluster headaches **Therapeutic Effects** Reduces migraine and cluster headache symptoms	**Drug Interactions** Selective serotonin reuptake inhibitors Serotonin and norepinephrine reuptake inhibitors Tricyclic antidepressants **Food Interactions** No significant interactions
Adverse Effects Paresthesia Drowsiness/sedation Nausea and vomiting Muscle weakness Fatigue Serotonin syndrome	**Contraindications** Hypersensitivity Caution: Monitor closely in clients who are taking other drugs associated with serotonin syndrome because coadministration of lasmiditan with these drugs can cause serotonin syndrome Monitor closely for central nervous system depression/impaired driving

TABLE 12.13 **Drug Prototype Table: Lasmiditan** (source: https://dailymed.nlm.nih.gov/dailymed/)

Calcitonin Gene Related Peptide (CGRP) Receptor Antagonists

Calcitonin gene related peptide (CGRP) receptor antagonists are a novel drug class used in the treatment of migraine headaches. They block CGRP receptors and inhibit the biological activity of CGRP neuropeptides. Adverse effects include nausea, rash, and dyspnea. Contraindications include hypersensitivity to the drug or its constituents (Rashid & Manghi, 2022).

The most prescribed CGRP receptor antagonist is rimegepant (Nurtec). Table 12.14 is a drug prototype table for CGRPs featuring rimegepant. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class CGRP receptor antagonist **Mechanism of Action** Binds to CGRP receptors, decreasing inflammation in the meninges of the brain	**Drug Dosage** Recommended dose is 75 mg orally as needed. *Maximum dose:* 75 mg in a 24-hour period.
Indications To treat migraine headaches **Therapeutic Effects** Reduces migraine headaches	**Drug Interactions** Ritonavir Indinavir Amiodarone Cyclosporine Quinidine **Food Interactions** No significant interactions
Adverse Effects Nausea Rash Shortness of breath	**Contraindications** Hypersensitivity Caution: Monitor closely in clients with hepatic insufficiency

TABLE 12.14 **Drug Prototype Table: Rimegepant** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking migraine headache drugs:

- Assess the client's medical history, current drug list, and allergies.
- Assess client's baseline symptoms, vital signs, and pain level.
- Ensure the drug is prepared appropriately using aseptic technique and verify dosage before administration.
- Monitor the client's response to the drug, including any changes in pain level, neurological status, and vital signs.
- Maintain a dark, calm, and quiet environment.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a migraine headache drug should:

- Get adequate sleep and rest.
- Keep a journal of symptoms, the presence or non-presence of an aura, and improved or worsening symptoms.
- Take migraine drugs as prescribed.
- Identify food triggers, environmental triggers, hormonal triggers, and stress triggers.
- Report worsening of symptoms such as visual changes and uncontrolled head pain to the health care provider immediately because these manifestations can be debilitating.

The client taking a migraine headache drug *should not*:

- Drink alcohol or smoke as these can precipitate symptoms of migraine headaches.
- Operate heavy equipment or machinery while taking migraine headache drugs.

12.3 Intracranial Emergencies and Intracranial Emergency Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 12.3.1 Describe the pathophysiology of common intracranial emergencies.
- 12.3.2 Identify the clinical manifestations related to common intracranial emergencies.
- 12.3.3 Identify the etiology and diagnostic studies related to common intracranial emergencies.
- 12.3.4 Identify the characteristics of drugs used to treat common intracranial emergencies.
- 12.3.5 Explain the indications, action, adverse reactions, and interactions of drugs used to treat common intracranial emergencies.
- 12.3.6 Describe nursing implications of drugs used to treat common intracranial emergencies.
- 12.3.7 Explain the client education related to drugs used to treat common intracranial emergencies.

Intracranial Emergency Overview

In adults, the brain has a constant volume, but the amount of **cerebrospinal fluid** and blood in the skull changes regularly to control pressure in the brain. Cerebrospinal fluid is produced by the brain and absorbed by the veins in the skull. Normal cerebrospinal fluid pressure varies with age but generally should not exceed 250 mm H_2O in adults (Sharma et al., 2023). The skull has a relatively fixed volume of approximately 1400–1700 mL (Cook, 2016), consisting of 80 percent brain parenchyma, 10 percent cerebrospinal fluid, and 10 percent blood. Any increase in the volume of components within the skull or an addition of a pathological element, such as a brain tumor, will result in increased pressure within the skull since the skull's volume is considered constant.

Intracranial emergencies encompass a range of sudden and serious medical conditions that affect the brain, its surrounding structures, or blood vessels within the skull (see Figure 12.3). These conditions can result from a variety of factors including head trauma, bleeding, blockage of blood vessels within the brain, head or sinus infections, brain tumors, or other underlying medical conditions. Successful treatment of intracranial emergencies requires early recognition and prompt medical intervention. Delayed treatment can lead to irreversible brain damage or death. This chapter will specifically delve into **intracranial hypertension** and **increased intracranial pressure**, providing an in-depth examination of their causes, symptoms, and treatment options.

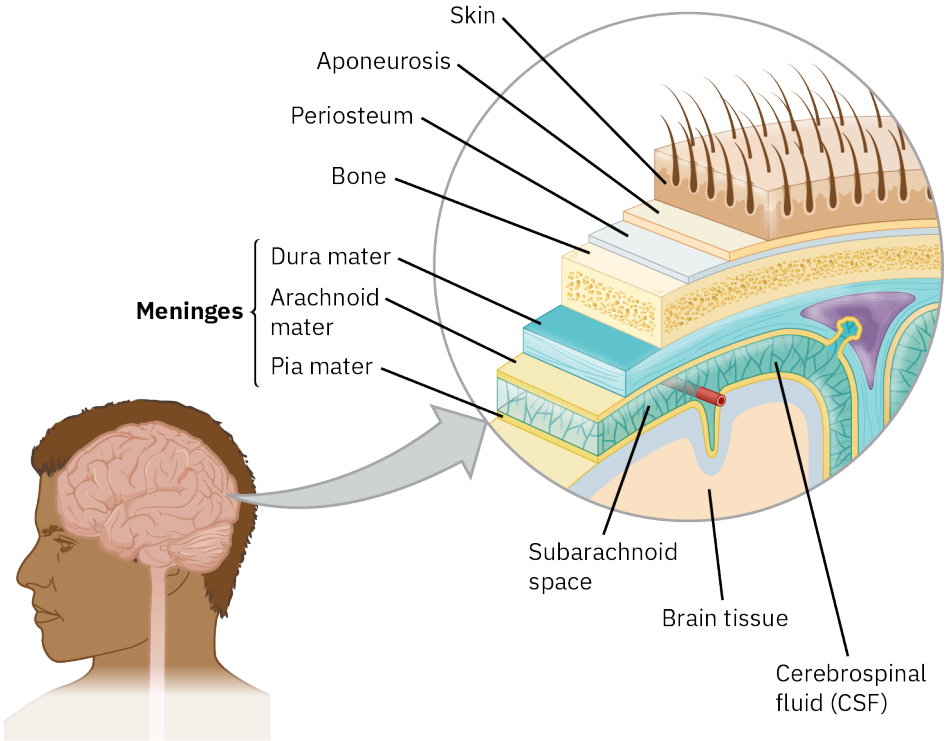


FIGURE 12.3 The layers of tissue surrounding the brain play an important role during intracranial emergencies, especially when there is an elevation in intracranial pressure. (credit: modification of work from *Microbiology*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Intracranial Hypertension and Increased Intracranial Pressure

Intracranial hypertension and increased intracranial pressure are related conditions, but they have distinct differences. Intracranial hypertension refers specifically to an elevated pressure within the skull that may or may not cause symptoms. However, increased intracranial pressure refers to a rise in the pressure within the skull that can cause various symptoms, such as headache, nausea, vomiting, visual changes, and altered mental status. Intracranial hypertension can be a cause of increased intracranial pressure, but it is not the only cause. Other factors that can lead to increased intracranial pressure include brain tumors, bleeding within the brain, infections, or trauma. Significantly, prompt recognition and management of increased intracranial pressure are critical to prevent irreversible brain damage and ensure the best possible outcomes for clients (Munakomi & Das, 2023).

Intracranial pressure is typically measured at the level of the **foramen of Monro** and is normally between 7 mm Hg and 15 mm Hg in vertically positioned adults. Intracranial hypertension is a clinical condition that is associated with an elevation of the pressures within the cranium. The cranial vault is measured in millimeters of mercury (mm Hg) and is normally less than 20 mm Hg (Pinto et al., 2022). Therapy to lower intracranial pressure should be initiated when increased intracranial pressure is greater than 20 mm Hg to 25 mm Hg (Munakomi & Das, 2023).

LINK TO LEARNING

Increased Intracranial Pressure

Access multimedia content (https://openstax.org/books/pharmacology/pages/12-3-intracranial-emergencies-and-intracranial-emergency-drugs)

Dr. Mike Todorovic and Dr. Matt Barton, senior lecturers and medical researchers at Griffith University, Australia, present an educational video on increased intracranial pressure.

Diagnostic Testing

Intracranial hypertension and increased intracranial pressure can be diagnosed with these tests:

- Neurologic assessment: A physical examination of the client's neurological function can provide information about the presence of increased pressure or fluid within the skull and brain.
- Radiologic imaging: CT and MRI are commonly used to evaluate the brain for structural abnormalities that may cause intracranial hypertension or increased intracranial pressure.
- **Intracranial pressure monitoring**: Direct measurement of intracranial pressure can be obtained by inserting a catheter into the skull and connecting it to a pressure transducer. This is the "gold standard" for diagnosing and monitoring increased intracranial pressure.
- Transcranial doppler: This is a noninvasive test that uses ultrasound to measure the velocity of blood flow in the brain's blood vessels. It can be used to assess cerebral blood flow and help diagnose and monitor increased intracranial pressure.
- **Ophthalmologic examination:** Increased intracranial pressure can cause swelling of the optic nerve, which can be detected by an ophthalmologist during an eye examination.

The choice of diagnostic test depends on the suspected cause of intracranial hypertension and increased intracranial pressure, the severity of the symptoms, and the availability of resources. A combination of these tests may be necessary to make an accurate diagnosis and to develop an appropriate plan of treatment.

Clinical Manifestations

Clinical manifestations of intracranial hypertension and increased intracranial pressure can vary depending on the underlying cause and the individual client factors. A thorough evaluation by a health care provider is necessary to accurately diagnose and manage these conditions.

Clinical manifestations of intracranial hypertension may include:

- Headache
- Nausea
- Blurred vision
- Dizziness

- Tinnitus
- Confusion or altered mental status

Clinical manifestations of increased intracranial pressure may include:

- Headache
- Seizures
- Papilledema
- Altered mental status, including drowsiness, confusion, or coma
- Changes in vital signs, such as bradycardia (slow heart rate) or hypertension

In severe cases, increased intracranial pressure can lead to **brain herniation**, a condition in which a portion of the brain is displaced due to increased intracranial pressure, a life-threatening condition. Symptoms of brain herniation can include changes in breathing pattern, dilation of one or both pupils, loss of consciousness, coma, and death.

CLINICAL TIP

Nursing Interventions to Lower/Stabilize Increased Intracranial Pressure

Along with administering drugs to decrease elevated intracranial pressure, the nurse must keep the head of the client's bed at a 30-degree angle, or as directed by the health care provider, and keep the client's neck in a neutral position to help stabilize and lower intracranial pressure (Faraj et al., 2022).

Drugs Used for Intracranial Emergencies

The health care provider selects drugs to treat intracranial hypertension and increased intracranial pressure based on the underlying cause and severity of the condition. For example, in some cases of **cerebral edema**, osmotic diuretics or carbonic anhydrase inhibitors (CAIs) may be used to reduce brain swelling and lower intracranial pressure. Non-pharmaceutical treatments—such as radiation or surgery—may also be needed as adjuvant treatment, particularly if there is a mass, tumor, bleeding, or trauma to the brain. The health care provider may also need to monitor the client's response to treatment and adjust the drug regimen accordingly. Common drugs used to treat issues with intracranial hypertension and increased intracranial pressure include glucocorticoids, hyperosmolar therapy (mannitol and hypertonic saline), barbiturates, sedatives, and antiepileptic drugs (Faraj et al., 2022). This section of the chapter will focus on drugs that are aimed at reducing intracranial pressure and cerebral edema including CAIs and osmotic diuretics.

Carbonic Anhydrase Inhibitors (CAIs)

CAIs are a class of drugs that are commonly used to treat a range of conditions, including intracranial hypertension, altitude sickness, and glaucoma. In managing intracranial emergencies, CAIs work by blocking carbonic anhydrase on the luminal membrane and inside the proximal renal tubule, which results in a reduction in the secretion of bicarbonate ions through the **sodium and hydrogen antiporter**. This decrease in bicarbonate ion secretion leads to a reduction in cerebrospinal fluid and intracranial pressure, making CAIs an important therapeutic option for managing intracranial hypertension (Aslam & Gupta, 2022).

Adverse effects of CAIs include changes in taste, fatigue, abdominal pain, nausea, diarrhea, blurred vision, tinnitus, paresthesia, rash, and headache. Serious adverse effects include hypokalemia, metabolic acidosis, aplastic anemia, **fulminant hepatic necrosis**, and **nephrolithiasis**. CAIs are contraindicated in clients with hepatic disease, in those with certain electrolytes imbalances—such as hypokalemia and hyponatremia—and in those with hypersensitivity to the drug or its components (Aslam & Gupta, 2022).

SAFETY ALERT

Aspirin and Acetazolamide

Caution is advised for client's receiving concomitant high-dose aspirin and acetazolamide, as anorexia, tachypnea, lethargy, metabolic acidosis, and death have been reported.

The most common CAI prescribed for intracranial hypertension is acetazolamide (Farzam & Abdullah, 2022). Table 12.15 is a drug prototype table for CAIs featuring acetazolamide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class CAI Diuretic **Mechanism of Action** Blocks carbonic anhydrase on the luminal membrane and inside the proximal renal tubule, decreasing bicarbonate ion secretion and thereby reducing cerebrospinal fluid and increased intracranial pressure	**Drug Dosage** Recommended dose is 500 mg 2 times daily (1 capsule in the morning and 1 capsule in the evening); may increase by 250 mg up to 4000 mg/day.
Indications To treat idiopathic intracranial hypertension Also used in the treatment of glaucoma, heart failure, altitude sickness, and epilepsy **Therapeutic Effects** Reduces edema	**Drug Interactions** Ritonavir Indinavir Amiodarone Cyclosporine Quinidine **Food Interactions** No significant interactions
Adverse Effects Headaches Malaise Fever Nausea/vomiting Aplastic anemia Fulminant hepatic necrosis Metabolic acidosis Paresthesia Nephrolithiasis Alterations in taste	**Contraindications** Hypersensitivity Hyponatremia Hypokalemia Hepatic disease Caution: Monitor closely in clients with hepatic and renal insufficiency and in those with certain electrolyte imbalances such as hyponatremia and hypokalemia

TABLE 12.15 **Drug Prototype Table: Acetazolamide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Osmotic Diuretics

Osmotic diuretics are a class of drugs that primarily function by inhibiting the reabsorption of water in the proximal convoluted tubule, the descending loop of Henle, and the collecting duct, all of which are regions of the kidney that are highly permeable to water. In addition to this mechanism, osmotic diuretics also extract water from the intracellular compartments, thereby increasing extracellular fluid volume, which results in a reduction in edema. Adverse effects include dehydration, heart failure due to the shift of free water, hyponatremia, hypokalemia, and hypocalcemia. Osmotic diuretics are contraindicated in clients with anuria due to renal disease, pulmonary edema, severe dehydration, progressive heart failure, and in those with hypersensitivity to the drug or any of its compounds (Tenny et al., 2022). More information on this topic is included in Diuretic Drugs.

Mannitol administration preparation should include inspecting the injection for particulate matter, discoloration, or crystallization before and periodically during administration. Discard the mannitol solution if particulates, crystallization, or discoloration are present.

Mannitol is the most prescribed osmotic diuretic indicated for decreasing cerebral edema. Table 12.16 is a drug prototype table for osmotic diuretics featuring mannitol. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Osmotic diuretic **Mechanism of Action** Causes osmosis from intracellular fluid (ICF) to extracellular fluid (ECF) by drawing water out of the brain parenchyma and into the intravascular space	**Drug Dosage** The total dosage, concentration, and rate of administration depend on the age, weight, and condition of the client being treated, including fluid requirement, electrolyte balance, serum osmolality, urinary output, and concomitant therapy. Monitor serum osmolarity. *Reduction of intracranial pressure:* Usually a maximum reduction in intracranial pressure in adults can be achieved with a dose of 0.25 g/kg/dose infused intravenously over 30 minutes, which may be repeated every 6–8 hours *Reduction of intraocular pressure:* The recommended dosage is 1.5–2 g/kg of a 20% solution (7.5–10 mL/kg) as a single dose infused intravenously over a period of at least 30 minutes. When used preoperatively, administer 1–1 ½ hours before surgery to achieve maximal reduction of intraocular pressure before the procedure.
Indications To treat increased intracranial pressure and cerebral edema To treat increased intraocular pressure **Therapeutic Effects** Reduces intracranial pressure and cerebral edema Decreases intraocular pressure	**Drug Interactions** Aminoglycosides Cyclosporine Digoxin Other diuretics **Food Interactions** No significant interactions
Adverse Effects Acute kidney injury Dehydration Headache Lethargy Confusion Metabolic acidosis Congestive heart failure Pulmonary edema Dry mouth Malaise Urticaria	**Contraindications** Hypersensitivity Anuria Severe hypovolemia Preexisting pulmonary edema Active intracranial bleeding except during craniotomy Caution: Monitor closely in clients who have congestive heart failure because this drug may cause volume overload from fluid shift

TABLE 12.16 **Drug Prototype Table: Mannitol** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are receiving mannitol or other intracranial emergency drugs:

- Before administering, assess the client's medical history, current drug list, and allergies.
- Administer the drug as prescribed by the health care provider.
- Observe and report symptoms of cerebral edema and intracranial hypertension to the health care provider. These symptoms include headache, confusion, dizziness, convulsions, unconsciousness, bradycardia, or failure of the pupils to react to light.
- Monitor laboratory tests to detect for possible complications of these drugs such as metabolic acidosis and electrolyte imbalances as hypo/hypernatremia and hypo/hyperkalemia.
- Monitor intake and output as well as urinary output in response to diuresis.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

If alert and oriented, the client receiving an emergency drug should:

- Be aware of signs of decreased intracranial pressure and cerebral edema, such as decreased confusion, improved coordination, decreased blood pressure, and increased urine output.
- Report symptoms of fluid retention including swelling in legs and feet, weight gain, and shortness of breath to their health care provider as these may represent an adverse reaction to the drug.

The client taking an intracranial emergency drug *should not*:

- Stop taking the drug unless directed by their health care provider, as this drug class may cause fluid shifts within the body resulting in shortness of breath, peripheral edema, and bradycardia.

Chapter Summary

This chapter provided an overview of epilepsy, migraine headaches, and intracranial emergencies. A brief pathophysiology was provided, as well as discussion on etiology, diagnostic testing, and clinical manifestations for each of the conditions.

Anticonvulsant drugs and drugs used to treat epilepsy were discussed. Common classifications of these drugs include hydantoins, barbiturates, succinates, benzodiazepines, iminostilbene, and valproates. An overview of nursing implications and client education was provided.

Drugs used to treat migraine headaches were briefly presented. Drug cases discussed included triptans, ergot alkaloids, selective serotonin receptor agonists, and CGRP receptor antagonists. Consideration was given to nursing implications and client education.

Additionally, drugs used in the treatment of intracranial hypertension and increased intracranial pressure during intracranial emergencies were presented, including CAIs and osmotic diuretics. Special consideration is given to nursing implications and client education for this drug classifications.

Key Terms

abortive therapy therapy that aims to relieve symptoms through drug administration

absence seizures seizures that cause rapid blinking or a few seconds of staring into space, also known as petit mal seizures

alpha-adrenergic blockers a class of drugs that bind and inhibit alpha-adrenergic receptors, thereby inhibiting smooth muscle contraction

anticonvulsant drugs drugs that are primarily used to treat seizures and epilepsy

aura terminology used to describe the warning signs of an impending seizure

brain herniation a life-threatening condition in which a portion of the brain is displaced due to increased intracranial pressure

cerebral edema swelling of the brain

cerebrospinal fluid a clear, colorless, watery fluid that flows in and around the brain and spinal cord

complex focal seizures a type of focal seizure that makes a person confused or dazed and unresponsive to questions or directions for up to a few minutes.

computed tomography (CT) scan a noninvasive imaging procedure that uses x-rays to produce horizontal and axial images of the brain

convulsions an involuntary contraction of muscles that cause sudden irregular movements of the body

electroencephalogram (EEG) a test that measures changes in the brain's electrical patterns that relate to seizures or other neurological conditions

epilepsy a neurological disorder characterized by recurrent seizures

focal seizures seizures that begin in a specific area of the brain and can cause a wide range of symptoms depending on the area of the brain that is affected; also known as partial seizures

foramen of Monro a short communication channel between the paired lateral ventricles and the third ventricle of the brain

fulminant hepatic necrosis terminology for acute liver failure

gamma aminobutyric acid (GABA) inhibitory neurotransmitter in the central nervous system

generalized seizures seizures in which abnormal activity occurs in both sides of the brain from the beginning of the seizure

gingival hyperplasia gum overgrowth

grand mal seizures seizures that involve both tonic (muscle stiffness) and clonic (muscle jerking) phases, also known as tonic-clonic seizures

headaches a prevalent medical condition that can cause pain or discomfort in the head or neck area

idiopathic seizure a seizure in which the cause cannot be identified

increased intracranial pressure a rise in the pressure within the skull that can cause various symptoms, such as headache, nausea, vomiting, visual changes, and altered mental status

intracranial emergencies a range of sudden and serious medical conditions that affect the brain, its surrounding structures, or blood vessels within the skull

intracranial hypertension an elevated pressure within the skull that may or may not cause symptoms

intracranial pressure monitoring direct measurement of intracranial pressure by inserting a catheter into the skull and connecting it to a pressure transducer

magnetic resonance imaging (MRI) an imaging procedure that uses large magnetic radio waves to produce clear images of the structures inside the skull

migraine headaches a type of headache that can be recurring and are often associated with a range of symptoms that can greatly affect quality of life

nephrolithiasis hard deposits of mineral and salts that form inside the kidney or urinary tract, also known as renal calculi or kidney stones

partial seizures seizures that begin in a specific area of the brain and can cause a wide range of symptoms depending on the area of the brain that is affected; also known as focal seizures

petit mal seizures seizures that cause rapid blinking or a few seconds of staring into space; also known as absence seizures

positron emission tomography (PET) scan an imaging procedure that uses a radioactive tracer substance to detect disease or injury in the brain

preventive therapy the use of drugs to prevent the occurrence of a condition

secondary generalized seizures seizures that begin in one part of the brain but then spread to both sides of the brain; the person first has a focal seizure, followed by a generalized seizure

seizure a sudden and temporary disturbance in the electrical activity of the brain that can cause changes in behavior, movement, or consciousness

serotonin agonists drugs that bind to and activate serotonin receptors, often used in the treatment of depression, anxiety, and migraine headaches

simple focal seizures seizures that affect a small part of the brain and cause twitching movements or a change in sensation, such as an odd taste or smell

sodium and hydrogen antiporter a membrane protein that transports sodium into the cell and hydrogen out of the cell

tonic-clonic seizures seizures that involve both tonic (muscle stiffness) and clonic (muscle jerking) phases, also known as grand mal seizures

Review Questions

1. A nurse is caring for a client who is receiving mannitol. Which of the following interventions should the nurse provide for the client?
   a. Elevate the head of the bed to 30 degrees and keep the client's head at a neutral position.
   b. Place the client in a supine position with the head turned to the right side.
   c. Elevate the head of the bed 90 degrees and keep the client's head at a neutral position.
   d. Place the client in a supine position with the head turned to the left side.

2. A nurse is preparing to administer valproic acid 300 mg orally twice daily. Available is valproic acid 250 mg/5 mL. How many milliliters should the nurse administer per dose? Round to the nearest whole number.
   a. 4 mL
   b. 5 mL
   c. 6 mL
   d. 7 mL

3. A nurse is teaching a female client diagnosed with migraine headaches about a new prescription for sumatriptan. Which of the following instructions should the nurse include?
   a. Take this medication every day to prevent migraine headaches.
   b. Use contraception while taking this medication.
   c. Take the drug every 30 minutes until the migraine headache subsides.
   d. Monitor blood pressure every 2 hours while taking this medication.

4. A nurse is assessing a client who is receiving valproic acid. What therapeutic response does the nurse expect to see from valproic acid?
   a. Decreased seizure activity
   b. Reduced intracranial hypertension
   c. Improved migraine headache
   d. Decreased intracranial pressure

5. A nurse is preparing to administer phenytoin 70 mg bolus to a client with a seizure disorder. The drug is supplied as a 50 mg/mL vial. How many milliliters should the nurse administer? Round to the nearest tenth.
   a. 1.25 mL
   b. 1.4 mL
   c. 1.55 mL
   d. 1.6 mL

6. A client is prescribed ethosuximide for seizures. Which of the following adverse effects should the nurse monitor the client for?
   a. Increased energy
   b. Constipation
   c. Sleeplessness
   d. Rash

7. Which of the following statements is true about migraine headaches?
   a. A two-course therapy approach of preventive and prophylactic therapies is required for migraine headaches.
   b. Clinical manifestations of migraine headaches can last several hours up to several days.
   c. Migraine headaches do not affect a client's quality of life or ability to perform activities of daily living.
   d. Migraine headaches are triggered by a calm, quiet, and dark environment.

8. A nurse is monitoring increased intracranial pressure on a client. Which of the following findings would represent an abnormal intracranial pressure for an adult client in a vertical position?
   a. 5 mm Hg
   b. 8 mm Hg
   c. 14 mm Hg
   d. 20 mm Hg

9. The nurse is providing instruction to a client with newly diagnosed intracranial hypertension with increased intracranial pressure. On which of the following drugs should the nurse provide client education?
   a. Acetazolamide
   b. Lorazepam
   c. Phenytoin
   d. Lasmiditan

10. Which of the following drugs is commonly prescribed to treat seizures and can cause behavioral and psychotic adverse effects?
   a. Carbamazepine
   b. Rimegepant
   c. Acetazolamide
   d. Levetiracetam

CHAPTER 13
Psychopharmacologic Drugs

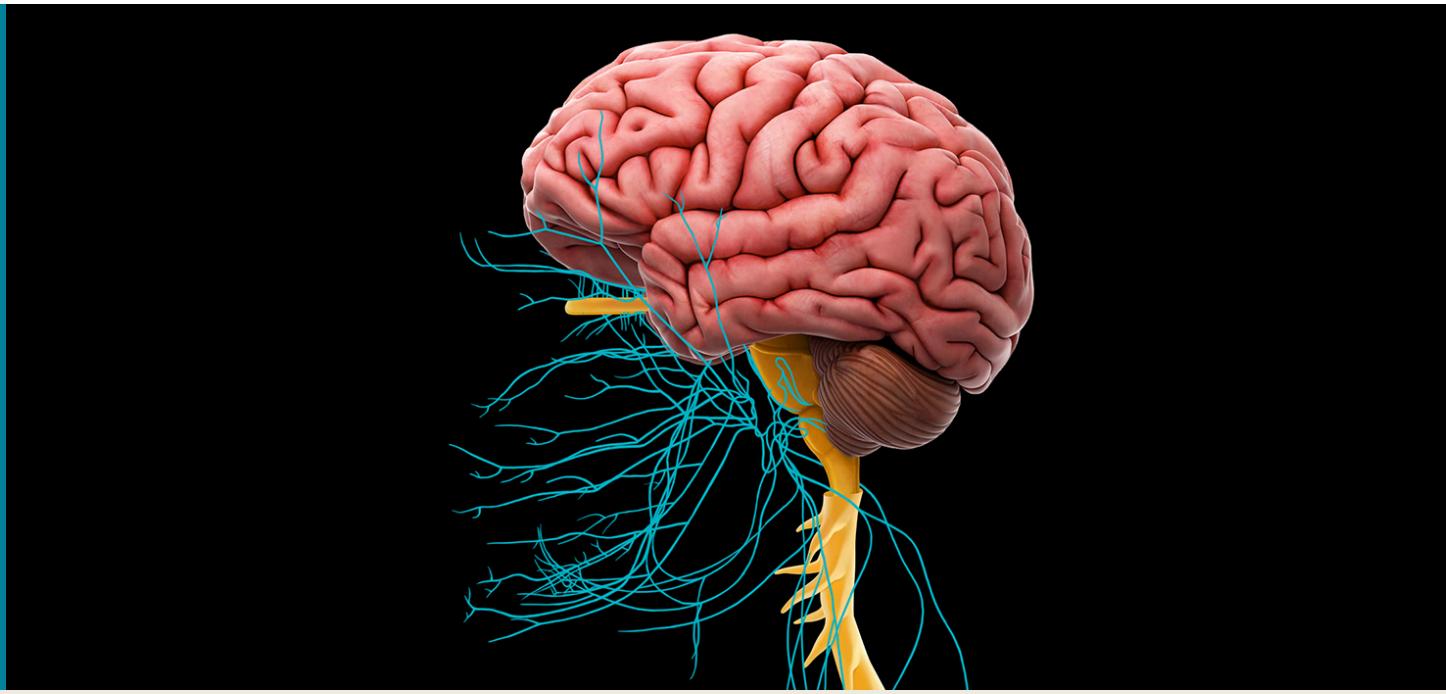


FIGURE 13.1 The nervous system, the body's control center, consists of the brain, the spinal cord, and a very complex system of nerves. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Nursing care of clients includes physical, spiritual, cultural, psychosocial, and psychological care. Many clients the nurse will work with will have current or past mental health issues that need to be considered when addressing their needs. Mental health includes our emotional, psychological, and social well-being. It affects how we think, feel, and act and also determines how we handle stress, relate to others, and make choices.

When an individual is diagnosed with a mental illness, nonpharmacologic therapies such as counseling or therapy often are used in combination with pharmacologic agents. **Psychopharmacology** is the use of **psychotropic medications** (drugs that affect mood, behaviors, thoughts, and perceptions) to treat mental illness. Psychotropic drugs target miscellaneous neurotransmitters and/or their receptors for effect. Drugs are mainly used to mitigate clinical manifestations of a psychological process. This chapter will focus on several of the common mental health disorders and their management.

13.1 Antidepressants

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 13.1.1 Identify the characteristics of drugs used to treat depression.
- 13.1.2 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat depression.
- 13.1.3 Describe nursing implications of drugs used to treat depression.
- 13.1.4 Explain the client education related to drugs used to treat depression.

Depression is an **affective** disorder in which the person experiences feelings of sadness, anger, frustration, hopelessness, and helplessness. Although most individuals can feel this way at any point in their lives, genuine clinical depressive symptoms significantly interfere with daily life over a sustained period. This condition does not discriminate and can affect all ages, races, sexes, and genders. According to the American Psychiatric Association (2022), the diagnostic criteria for major depressive disorder (MDD) is having five or more symptoms present during the same 2-week period, and it represents a change from previous function. At least one of the symptoms is either depressed mood most of the day nearly every day or loss of interest or pleasure. Other depressive symptoms include significant changes in weight or appetite, insomnia or **hypersomnia**, observable psychomotor agitation or retardation, fatigue, feelings of worthlessness or excessive and/or inappropriate guilt, diminished ability to think or concentrate, difficulty with decision making, and recurrent thoughts of death. Additionally, the symptoms cause clinically significant distress or impairment and are not in response to a significant loss, a medical condition, or the effects of substance use.

The pathophysiology of depression is not well understood. Clients may need to try different medications before finding one that improves their symptoms with the fewest side effects. Research is ongoing to better understand the biochemical changes that occur with depression and, accordingly, which antidepressant medications are the most effective. Nurses who work with clients taking these medications should monitor current research and clinical guidelines for the most up-to-date findings and recommendations.

SPECIAL CONSIDERATIONS

Racial and Ethnic Considerations

Studies have shown there are differences in antidepressant responses in populations of color. These differences are mainly related to genetic or ethnic variations in the **cytochrome P450 enzyme system** responsible for the metabolism of most drugs.

- Black clients tend to have higher plasma drug levels for a given dose, respond more rapidly, experience a higher incidence of adverse drug reactions (ADRs), and metabolize tricyclic antidepressants more slowly than White clients.
- Asian clients metabolize antidepressants more slowly than White clients. Based on current studies, Asian clients are generally considered to not metabolize antidepressants as quickly as clients from other racial and ethnic backgrounds. Metabolism is important for preparing the drug for excretion. If metabolism is inadequate, the drug accumulates in the plasma, and elevated drug levels induce toxicity.

(Source: Marazziti et al., 2021)

Tricyclic Antidepressants (TCAs)

Tricyclic antidepressants (TCAs) were introduced in the late 1950s. For decades, these were the drugs of choice to treat depression. Although they have been very effective over the years, they have some serious adverse drug reactions (ADRs), including **cardiotoxicity**. Therefore, today they are considered second-line drugs. If a client was able to tolerate a TCA in the past and it was effective, this may be the basis for selecting a TCA over a different class.

Tricyclic antidepressants, in low doses, are frequently used for other indications, such as neuropathy and insomnia.

Adverse Effects and Contraindications

Tricyclic antidepressants block acetylcholine (muscarinic) receptors; therefore, blurred vision, dry mouth,

constipation, and urine retention are common due to the anticholinergic properties. In addition, because they block histamine receptors, sedation and weight gain occur. Due to the blockade of alpha-1 adrenergic receptors, sedation and hypotension are common adverse effects. TCAs decrease vagal influence on the heart secondary to muscarinic blockade and act directly on the bundle of His to slow conduction. These drugs decrease the seizure threshold due to the blocking of ion channels, which can lead to the occurrence of seizures. Clients with a seizure disorder may need a dose increase for their antiseizure medication. Glaucoma is a contraindication because the anticholinergic properties can increase intraocular pressure (IOP).

Medications that lower the seizure threshold may increase the risk of seizures in clients taking TCAs. Concurrent use of TCAs with other anticholinergic and central nervous system (CNS) depressant drugs can worsen those effects. Certain antipsychotics can increase amitriptyline concentrations, and use of monoamine oxidase inhibitors (MAOIs) should be separated by 2 weeks due to the risk for serotonin syndrome (described in the following section). Because TCAs can prolong the heart's QTc interval, use with caution in clients who have bradycardia, who are taking drugs that can induce bradycardia, or who have electrolyte abnormalities that could result in a life-threatening dysrhythmia.

Table 13.1 is a drug prototype table for tricyclic antidepressants featuring amitriptyline. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Tricyclic antidepressant **Mechanism of Action** Blocks the reuptake of norepinephrine (NE) and serotonin at the presynaptic nerve endings	**Drug Dosage** *Adults:* Initial dose: 25–50 mg/day orally at bedtime. Increase dose by 25 mg every 3–7 days. Maximum dose: 300 mg. Can be taken at one time or in divided doses. *Adolescents (ages 12–17):* 10 mg orally 3 times daily and 20 mg orally at bedtime.
Indications Major depressive disorder (MDD) Primary insomnia Anxiety Chronic pain syndromes **Therapeutic Effects** Increases the effects of both NE and serotonin Can increase dopamine neurotransmission in the frontal cortex	**Drug Interactions** Tramadol Anticholinergic agents Fluvoxamine Phenothiazines or haloperidol Monoamine oxidase inhibitors (MAOIs) Calcium channel blockers/beta blockers/digoxin CNS depressants (opioids, antihistamines) **Food Interactions** No significant interactions
Adverse Effects Prolongation of QTc interval Tachycardia Dysrhythmias Sedation Dry mouth Blurred vision Urine retention/constipation Weight gain Hypotension Seizures Photosensitization	**Contraindications** Children <12 years Recent myocardial infarction Uncompensated heart failure Cardiac dysrhythmia Caution: Seizures Urinary retention/benign prostatic hyperplasia (BPH) Angle-closure glaucoma

TABLE 13.1 **Drug Prototype Table: Amitriptyline Hydrochloride** (source: https://dailymed.nlm.nih.gov/dailymed/)

Selective Serotonin Reuptake Inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressants. All are indicated

for major depression. Several of these medications are also prescribed "off-label" for other psychiatric disorders, meaning the prescriber is using them for purposes other than what they were approved for by the Food and Drug Administration (FDA) but still based upon scientific rationale (Van Norman, 2023). Normally, the actions of serotonin are terminated by active reuptake back into the nerve terminals from which it was released. By inhibiting the reuptake pump, the SSRIs cause serotonin to accumulate in the synaptic space. SSRIs have little effect on other neurotransmitters and accordingly cause fewer adverse effects (Chu & Wadhwa, 2023). The most common SSRIs include:

- *Citalopram:* This drug is FDA approved only for major depression; however, it is used off-label for other conditions.
- *Paroxetine:* In addition to major depression, this drug is used for obsessive-compulsive disorder (OCD), panic disorder, social phobia, generalized anxiety disorder (GAD), posttraumatic stress disorder (PTSD), and premenstrual dysphoric disorder (PMDD).
- *Fluoxetine:* This drug is used for major depression, OCD, panic disorder, PMDD, and bulimia nervosa. Fluoxetine does not block receptors for histamine, NE, or acetylcholine; therefore, the drug does not cause sedation, orthostatic hypotension, anticholinergic effects, or cardiotoxicity.
- *Sertraline hydrochloride:* This is FDA approved for major depression, PMDD, OCD, PTSD, social anxiety disorder, and panic disorder.
- *Escitalopram:* This drug is FDA approved for GAD in addition to the indications listed for fluoxetine.

Table 13.2 lists common SSRIs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Citalopram (Celexa)	*Adults:* Initial dose: 20 mg/day orally; maximum dose: 40 mg/day. *Older adults (>60 years):* 20 mg orally daily.
Escitalopram (Lexapro)	*Adults:* 10 mg/day orally; may increase to maximum dose of 20 mg/day after a minimum of 1 week of therapy. *Adolescents 12–17 years:* 10 mg/day orally; may increase to maximum dose of 20 mg/day if symptoms do not lessen within 3 weeks of therapy.
Fluoxetine (Prozac)	*Adults:* *Immediate-release capsules:* 20 mg orally once daily in the morning; may increase after several weeks if necessary; maximum dose: 80 mg/day. *Delayed-release capsules:* 90 mg orally weekly, starting 7 days after the last 20 mg immediate dose. *Adolescents 12–17 years:* *Immediate-release capsules:* 10 mg/day orally; may increase to 20 mg/day after 1 week if necessary.
Paroxetine (Paxil)	*Adults:* *Immediate-release tablets:* 20 mg orally once daily in the morning; increase dose at 1-week intervals if necessary; usual range: 20–50 mg/day; maximum dose: 50 mg/day. *Controlled-release tablets:* 25 mg orally once daily in the morning; maximum dose: 62.5 mg/day. *Older adults (>60 years):* *Immediate-release tablets:* 10 mg orally once daily in the morning; maximum dose: 40 mg/day.
Sertraline (Zoloft)	*Adults:* 50 mg orally once daily morning or evening; may increase dose at 1-week intervals if necessary; maximum dose: 200 mg/day.

TABLE 13.2 **Drug Emphasis Table: Selective Serotonin Reuptake Inhibitors** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Sexual dysfunction is one main reason why clients may elect to stop taking SSRIs. Impotence, delayed or absent ejaculation or orgasm, and decreased libido can be side effects of these medications. This can be managed in several ways: reduction of the dose, taking drug holidays, or adding a drug that can overcome the problem. Weight gain can occur due to the decreased sensitivity of serotonin receptors that regulate appetite.

MAOIs and fluoxetine should be separated at least 5 weeks apart to prevent serotonin syndrome. The remaining

SSRIs and MAOIs should be separated by 2 weeks. This is due to the long half-life of fluoxetine. Serotonin syndrome is characterized by altered mental status, anxiety, hallucinations, **hyperpyrexia**, muscle rigidity, hyperreflexia, diaphoresis, and tremor. Tramadol also can increase the risk of serotonin syndrome when combined with SSRIs. The syndrome will resolve spontaneously after the drug(s) have been stopped.

Fluoxetine and other SSRIs can increase the risk of gastrointestinal (GI) bleeding either by impeding platelet aggregation or by increasing gastric acidity (Edinoff et al., 2022). These drugs can increase the risk for bleeding, so caution needs to be exercised for clients taking aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and anticoagulants because these can further the risk of bleeding. Fluoxetine also has CNS stimulant effects, which can cause insomnia and anxiety.

Table 13.3 is a drug prototype table for SSRIs featuring fluoxetine. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Selective serotonin reuptake inhibitor **Mechanism of Action** Selectively blocks neuronal reuptake of serotonin; over time, adaptive cellular changes take place in response to prolonged reuptake blockade	**Drug Dosage** *Adults:* *Immediate-release capsules:* 20 mg orally once daily in the morning; may increase after several weeks if necessary; maximum dose: 80 mg/day. *Delayed-release capsules:* 90 mg orally weekly, starting 7 days after the last 20 mg immediate dose. *Adolescents 12–17 years:* *Immediate-release capsules:* 10 mg/day orally; may increase to 20 mg/day after 1 week if necessary.
Indications Major depression (≥8 years of age) OCD (≥7 years of age) Panic disorder PMDD Bulimia nervosa Bipolar depression (in combination with olanzapine) Treatment-resistant depression (in combination with olanzapine) **Therapeutic Effects** Concentration of serotonin in the synapse increases, resulting in enhanced activation of postsynaptic serotonin receptors	**Drug Interactions** Tramadol MAOIs Warfarin Aspirin NSAIDs **Food Interactions** No significant interactions
Adverse Effects Nausea Headache Insomnia Nervousness Sexual dysfunction Weight gain Suicidal ideations (especially in children/adolescents)	**Contraindications** Hypersensitivity Caution: GI ulcers History of GI bleeding Adults >60 years of age

TABLE 13.3 **Drug Prototype Table: Fluoxetine** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Similarly Named Drugs Associated with SSRIs

Do not confuse:

- Celexa (SSRI) with Celebrex (proton pump inhibitor) or Zyprexa (antipsychotic)

- Fluoxetine (SSRI) with loxitane (antipsychotic)
- Prozac (SSRI) with Prograf (immunosuppressant), Provera (progesterone hormone), or Prilosec (proton pump inhibitor)
- Paxil (SSRI) with Plavix (antiplatelet) or Taxol (chemotherapy)
- Sertraline (SSRI) with cetirizine (histamine-1 receptor antagonist)

(Source: Institute for Safe Medication Practices [ISMP], 2023)

Serotonin Norepinephrine Reuptake Inhibitors

Besides blocking norepinephrine (NE) and serotonin, serotonin norepinephrine reuptake inhibitors (SNRIs) have minimal effects on other transmitters or receptors. SNRIs increase the levels of serotonin and NE in the brain, which play an important role in mood. These drugs can also weakly inhibit dopamine reuptake. Pharmacological effects are similar to the SSRIs. The most common SNRIs are:

- *Venlafaxine:* Used in major depression, panic disorder, social phobia, and GAD
- *Duloxetine:* Used for MDD, diabetic peripheral neuropathic pain, fibromyalgia, GAD, social anxiety, panic disorder, and chronic musculoskeletal pain in adults; used for depression, GAD, and fibromyalgia in children
- *Levomilnacipran:* FDA approved only for major depression but used off-label for GAD and chronic pain disorder

Table 13.4 lists common SNRIs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Venlafaxine (Effexor)	*Adults:* Initial dose: 37.5 mg/day (extended release) or 25–50 mg divided into 2–3 doses (immediate release) for 1 week; increase daily dose no faster than 75 mg every 4 days until desired response is optimal; maximum dose: 225 mg/day.
Duloxetine (Cymbalta)	*MDD in adults:* Initial dose: 40 mg/day orally in 2 doses; can increase to 60 mg/day in 1–2 doses if necessary; maximum dose: 120 mg/day. *GAD in adults:* 30–60 mg/day orally in capsules; maximum dose: 120 mg/day orally. *MDD and GAD in children (7–17 years):* 30 mg orally once daily; maximum dose: 120 mg/day.
Levomilnacipran (Fetzima)	*Adults:* Initial dose: 20 mg/day orally for 2 days, then increase to 40 mg/day; can increase by 40 mg/day every 2 or more days; maximum dose: 120 mg/day.

TABLE 13.4 Drug Emphasis Table: Serotonin Norepinephrine Reuptake Inhibitors (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Similar to most SSRIs, SNRIs should not be taken until the client has stopped taking MAOIs for at least 14 days. This is to decrease the risk of serotonin syndrome.

Neonatal syndrome can occur when duloxetine is taken late in pregnancy. This syndrome is characterized by irritability, high-pitched cry, tremor, respiratory distress, and possible seizures in the neonate.

Use with caution for clients who have **bipolar disorder**, unless they are treated with a concomitant mood-stabilizing agent.

SNRIs have the potential to increase blood pressure; therefore, anyone with uncontrolled hypertension should avoid this class of drugs. Unwanted effects of insomnia, decreased appetite, increased blood pressure, and urinary retention can occur when the levels of serotonin and NE become elevated in certain parts of the brain and periphery that play no role in inducing the therapeutic effects.

Table 13.5 is a drug prototype table for SNRIs featuring duloxetine. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Serotonin norepinephrine reuptake inhibitor **Mechanism of Action** Powerful blockade of NE and serotonin reuptake Weak blockade of dopamine reuptake	**Drug Dosage** *MDD in adults:* Initial dose: 40 mg/day orally in 2 doses; can increase to 60 mg/day in 1–2 doses if necessary; maximum dose: 120 mg/day. *GAD in adults:* 30–60 mg/day orally in capsules; maximum dose: 120 mg/day orally. *MDD and GAD in children (7–17 years):* 30 mg orally once daily; maximum dose: 120 mg/day.
Indications MDD Diabetic peripheral neuropathic pain Fibromyalgia GAD Social anxiety Panic disorder Chronic musculoskeletal pain **Therapeutic Effects** Increases concentration of NE and dopamine in the brain	**Drug Interactions** MAOIs Antiplatelet agents Anticoagulants **Food Interactions** No significant interactions
Adverse Effects Nausea Headache Anxiety/nervousness Hyperhidrosis (excessive sweating) Insomnia Hepatotoxicity Weight loss (dose-dependent) Sexual dysfunction Elevated blood pressure Urinary retention Neonatal withdrawal syndrome Suicidal ideations (especially in children) Seizures	**Contraindications** None Caution: Significant hepatic dysfunction Orthostatic hypotension Angle-closure glaucoma Substantial alcohol user Uncontrolled hypertension Seizure disorders Bipolar disorder Hyponatremia Depression/suicidal ideations in children, adolescents, and young adults

TABLE 13.5 **Drug Prototype Table: Duloxetine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Norepinephrine Dopamine Reuptake Inhibitors

Norepinephrine dopamine reuptake inhibitors (NDRIs) inhibit the reuptake of dopamine, NE, and serotonin. Several metabolites are active, giving this class a prolonged duration of action. The most common drug in this class is bupropion hydrochloride (Aplenzin, Wellbutrin, Zyban). It is used for depression, seasonal affective disorder (SAD), and smoking cessation and as an adjunct to other antidepressants if the client did not obtain a full therapeutic response with them.

Adverse Effects and Contraindications

NDRIs have several CNS stimulant effects including agitation, anxiety, excitement, increased motor activity, and restlessness. These effects usually occur during the first few days of treatment. (The client may require a sedative for the first few days.) These effects occur because this drug is similar in structure to amphetamines. These effects also could potentially increase the risk of misuse.

The dose must be reduced with any impaired hepatic or renal function. Clients should be screened for bipolar disorder before starting therapy to prevent mania or hypomania. When the drug is being used for smoking cessation, it can cause neuropsychiatric adverse effects. Postmarketing reports include serious or clinically significant changes in mood (including depression and mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, aggression, hostility, agitation, anxiety, and panic as well as suicidal ideation, suicide attempt, and death by suicide

(DailyMed, *Bupropion*, 2023). This drug should be used cautiously in clients with a history of psychosis.

Unlike other antidepressants, this class does not cause sexual dysfunction or orthostatic hypotension.

A higher incidence of seizures was observed in clients being treated with the immediate-release formulation who have a current or past diagnosis of anorexia or bulimia nervosa. In addition, clients with a history of seizure disorders may need their drug dosages modified because bupropion decreases the seizure threshold and could trigger seizure activity.

The SSRIs listed in Table 13.2 inhibit the metabolism of bupropion; therefore, bupropion levels are increased, which increases the risk of seizures. MAOIs can increase the risk for bupropion toxicity as well as increase the risk of hypertensive crisis. Clients should discontinue MAOIs at least 2 weeks before starting bupropion.

Table 13.6 is a drug prototype table for NDRIs featuring bupropion hydrochloride. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Norepinephrine dopamine reuptake inhibitor **Mechanism of Action** Inhibits the reuptake of dopamine, norepinephrine, and serotonin	**Drug Dosage** *Immediate release:* Initial dose: 75 mg orally twice daily, increasing to 100 mg twice daily, and then 100 mg 3 times daily. Maximum dose: 450 mg/day. *Extended release:* Initial dose: 150 mg/day; can increase to 300 mg/day after 4 days; maximum dose: 400 mg/day. *Sustained release:* 100 mg orally twice daily; increase to 150 mg after 3 days; maximum dose: 400 mg/day.
Indications Depression SAD Smoking cessation **Therapeutic Effects** Increases the levels of dopamine, NE, and serotonin	**Drug Interactions** Sertraline Fluoxetine Paroxetine MAOIs used within 14 days **Food Interactions** No significant interactions
Adverse Effects Seizures Activation of mania/hypomania Neuropsychiatric effects Insomnia/tremors Tachycardia Increase in blood pressure Dry mouth Headache Constipation/nausea/vomiting Anorexia/weight loss Photosensitivity	**Contraindications** Hypersensitivity Seizures Conditions that may lower seizure threshold (anorexia/bulimia nervosa, alcohol/substance withdrawal) Caution: History of psychosis Impaired hepatic function Impaired renal function Hyperthyroidism Hypertension

TABLE 13.6 Drug Prototype Table: Bupropion Hydrochloride (source: https://dailymed.nlm.nih.gov/dailymed/)

Monoamine Oxidase Inhibitors

Monoamine oxidase inhibitors (MAOIs) are third-line agents for treating depression. MAOIs are not often used in practice today, mainly because of the numerous food and drug interactions that produce severe hypertension. Blood pressure could be elevated enough to cause a stroke or myocardial infarction. MAOIs are used when other antidepressants have been unsuccessful. The most common MAOIs are:

- *Phenelzine sulfate:* Used to treat major depression.
- *Selegiline hydrochloride:* This is the first and only transdermal treatment for major depression. It is a potent

irreversible MAOI with a great affinity for MAO-B in the brain at therapeutic doses. At higher doses, the drug becomes nonselective and can inhibit both MAO-A and MAO-B. It increases dopaminergic activity by interfering with dopamine reuptake at the synapse.

Table 13.7 lists common MAOIs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Phenelzine sulfate (Nardil)	15 mg orally 3 times daily; maximum dose: 90 mg/day.
Selegiline (Emsam)	6 mg/24 hours transdermally; may titrate based on clinical response in increments of 3 mg/day every 2 weeks; maximum dose: 12 mg/24 hours.

TABLE 13.7 Drug Emphasis Table: Monoamine Oxidase Inhibitors (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

MAOIs are contraindicated in older adults due to their high risk of diminished hepatic, renal, and cardiac function.

Tyramine is a **monoamine** precursor of NE. Normally, tyramine is deactivated in the GI tract and liver by the monoamine oxidase enzyme to avoid large amounts reaching the systemic circulation. Because these drugs block the monoamine oxidase enzyme, tyramine is absorbed systemically. It is transported to the adrenergic nerve terminals, where it causes a sudden release of significant amounts of NE. This NE activates the sympathetic nervous system.

The antidepressants listed here can increase the risk of serotonin syndrome. Vasoconstrictors and sympathomimetics can intensify the hypertensive effect. The use of opioids and MAOIs can result in hyperpyrexia (high fever). Caffeine can also exacerbate the CNS stimulatory effect. Blood glucose levels may decrease with MAOIs, resulting in hypoglycemic effects. In addition, MAOIs can enhance insulin receptor sensitivity, compounding the hypoglycemic state. A decrease in dosage may be necessary.

Table 13.8 is a drug prototype table for MAOIs featuring phenelzine sulfate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Monoamine oxidase inhibitor **Mechanism of Action** Irreversibly binds to the MAO-A enzyme	**Drug Dosage** 15 mg orally 3 times daily; maximum dose: 90 mg/day.
Indications Major depression **Therapeutic Effects** Increases and enhances the effect of norepinephrine, dopamine, and serotonin	**Drug Interactions** Antidepressants (TCAs, SSRIs, SNRIs, bupropion, carbamazepine) Vasoconstrictors Sympathomimetics (amphetamines, dextromethorphan, and diet pills) Opioids Insulin **Food Interactions** Caffeine Foods high in tyramine (milk, turkey, chicken, oats, seeds, soy products, seafood, canned tuna, aged cheeses, brewer's yeast, whole-wheat bread)
Adverse Effects Hypertensive crisis (headache, tachycardia, nausea and vomiting) Dysrhythmias CNS stimulation (insomnia, anxiety, agitation) Hepatotoxicity Orthostatic hypotension Sexual dysfunction Dizziness	**Contraindications** Severe hepatic disease Pheochromocytoma (adrenal tumor) Congestive heart failure Hypersensitivity to the drug or its ingredients Caution: Renal impairment Hepatic insufficiency Older adults

TABLE 13.8 **Drug Prototype Table: Phenelzine Sulfate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Miscellaneous Antidepressants

Some drugs work just as well for depressive symptoms but do not fit into the criteria of other drug classes. They include:

- *Mirtazapine:* Used to treat major depressive disorder.
- *Trazodone hydrochloride:* This drug is a serotonin 2 antagonist/reuptake inhibitor. It increases the amount of serotonin available. It is more frequently used for sedation and sleep than for depression. High doses are needed for antidepressant effects; however, these doses cause significant sedation. The drug is often concurrently administered with a stimulating antidepressant such as bupropion.
- *Vortioxetine:* Increases the release of several neurotransmitters (serotonin, NE, dopamine, glutamate, acetylcholine, and histamine). In addition, it reduces the release of GABA, a neurotransmitter that inhibits mood-related neurotransmitters, through three different modes of action.

Table 13.9 lists common miscellaneous antidepressants and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Mirtazapine (Remeron)	Initial dose: 15 mg/day orally in the evening; increase every 1–2 weeks until desired effect is achieved; maximum dose: 45 mg/day.
Trazodone hydrochloride (Desyrel)	Initial dose: 150 mg/day orally in divided doses; can increase by 50 mg/day every 3–4 days; maximum dose: 400 mg/day divided into 2 doses.
Vortioxetine (Trintellix)	Initial dose: 10 mg/day orally; can increase to 20 mg/day or decrease to 5 mg/day.

TABLE 13.9 Drug Emphasis Table: Miscellaneous Antidepressants (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

The antihistamine effects of mirtazapine and trazodone hydrochloride cause sedation and weight gain. Agranulocytosis is an identified adverse effect. If a client experiences generalized malaise, chills, fever, or myalgia, similar to the flu, this may indicate a low white blood cell (WBC) count. The provider should be notified. Because mirtazapine is associated with significant weight gain, clients should be weighed prior to starting the drug to determine their body mass index (BMI). If they are deemed to have overweight or obesity, it is important to identify whether the client is prediabetic or diabetic and/or dyslipidemic. If so, clients should be treated or referred for therapy.

Any of the miscellaneous antidepressants can cause a fatal serotonin syndrome when combined with MAOIs. Do not use with MAOIs or within 14 days after they have been discontinued. Drugs such as benzodiazepines, opioids, and antihistamines can increase the sedative properties.

Table 13.10 is a drug prototype table for miscellaneous antidepressants featuring mirtazapine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Miscellaneous antidepressant **Mechanism of Action** Blocks alpha-2 adrenergic presynaptic receptors, increasing NE neurotransmission Blocks alpha-2 adrenergic presynaptic receptor on serotonin neurons, leading to an increase in serotonin levels Blocks histamine-1 receptors	**Drug Dosage** Initial dose: 15 mg/day orally in the evening; increase every 1–2 weeks until desired effect is achieved; maximum dose: 45 mg/day.
Indications Major depressive disorder **Therapeutic Effects** Increased levels of NE and serotonin	**Drug Interactions** MAOIs Benzodiazepines/opioids/antihistamines **Food Interactions** No significant interactions
Adverse Effects Sedation Weight gain Increased appetite Elevates cholesterol and triglyceride levels Hypotension Malaise, fever, sore throat, myalgia, chills Leukopenia (low WBC count)	**Contraindications** Hypersensitivity to the drug or any of its ingredients Severe neutropenia Caution: Dyslipidemia Angle-closure glaucoma Risk factors for QT prolongation Seizures Hyponatremia Impaired hepatic function Bipolar disorder Depression/suicidal ideations in adolescents and young adults

TABLE 13.10 **Drug Prototype Table: Mirtazapine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antidepressants:

- Obtain orders for baseline testing prior to the client starting the medication and continue during treatment to monitor for side effects: an electrocardiogram for clients over age 50 and lab work (complete blood count [CBC], electrolytes, lipid panel, liver function tests, and HgbA1C). If client is on anticoagulants, such as warfarin, monitor PT/INR frequently.
- Obtain baseline weight and body mass index (BMI) and monitor throughout treatment.
- Monitor blood pressure and heart rate twice weekly during treatment.
- Monitor for signs and symptoms of mania or hypomania.
- Check mood and anxiety periodically during treatment.
- Monitor for seizure activity.
- Ensure safety precautions are in place due to sedation.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antidepressant should:

- Be aware that these drugs can take 2 weeks to start seeing effects and 4–6 weeks for full therapeutic

effects.
- Be informed about the high probability of sexual dysfunction and told to report any problems so they can be appropriately addressed.
- Immediately notify their provider about any clinical manifestations of increased depression or suicidal ideations.
- Contact their provider with signs of diabetes, such as increased thirst (polydipsia), extreme hunger (polyphagia), or increased urination (polyuria).
- Report signs of sore throat and/or fever.
- Assess for any signs of bleeding such as blood in urine (hematuria); dark, tarry stools; easy bruising; nosebleed (epistaxis); or bleeding gums.
- Notify their provider if there are any signs of liver disease, such as right upper quadrant pain, light-colored stools, and dark urine.

The client taking an antidepressant *should not:*

- Drive or engage in activities that require alertness until the effects of the medication are known.
- Eat foods high in tyramine (milk, turkey, chicken, oats, seeds, soy products, seafood, canned tuna, aged cheeses, brewer's yeast, whole-wheat bread) if using an MAOI.
- Be in direct sunlight without appropriate clothing and sunscreen.
- Take aspirin or NSAIDs.

FDA BLACK BOX WARNING

Antidepressants

In short-term trials, antidepressant use for major depressive disorder increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults under age 24 when compared to placebos. These trials did not show an increase in the risk of suicidal thoughts and behavior in individuals over age 24. There was a reduction in risk with antidepressant use in individuals ages 65 and older.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Jadalyn Sanchez is a 21-year-old female student who arrives at the university's student health center with complaints of frequent crying throughout the day and lack of motivation or interest in being with friends or engaging in activities she used to enjoy. She describes a sense of helplessness and inadequacy at school. Jadalyn states it takes everything for her to get out of bed to attend classes. She has had no appetite and lost 12 pounds over the past month. She reports that her symptoms have been present for approximately 6 weeks. She denies any recent or past traumatic events or losses. She reports occasional dating but currently is not in any committed relationship. She is sexually active and states that she is compliant with her prescribed oral contraceptives. She denies tobacco or illicit drug use and says she drinks two or three 6 oz glasses of wine on the weekends. She does not recall being this sad in the past. She states normally she is very active, meets all due dates, and takes her academics very seriously. Her roommate talked her into coming to the center because of the drastic change.

Family History
Mother (age 50): History of depression
Father (age 54): History of hypertension and bipolar disorder
Sister (age 24): Panic disorder and ADHD
Brother (age 16): ADHD and GAD

Current Medications

Loestrin Fe 1/20, once daily

Vital Signs		Physical Examination
Temperature:	97.6°F	• *Head, ears, eyes, nose, throat (HEENT):* Normocephalic, bilateral eyes red and puffy, positive clear nasal drainage, and minimal eye contact. Ears and throat unremarkable. No lymphadenopathy. Thyroid nonpalpable with positive rise upon swallowing. • *Cardiovascular:* Audible S1, S2. Rhythm regular. No murmurs, rubs, or gallops. No peripheral edema bilaterally. Radial and DP pulses 2+. • *Respiratory:* Lungs clear bilaterally in all fields. No use of accessory muscles. • *Gastrointestinal:* Abdomen round, soft, and nontender. Bowel sounds present in all four quadrants. • *Musculoskeletal:* Active and full range of motion in bilateral upper extremities and lower extremities with 5/5 muscle strength.
Blood pressure:	106/68 mm Hg	
Heart rate:	74 beats/min	
Respiratory rate:	16 breaths/min	
Oxygen saturation:	98% on room air	
Height:	5'5"	
Weight:	124 lb	

TABLE 13.11

1. Jadalyn was prescribed fluoxetine 20 mg once daily. What is an important point for the nurse to emphasize to Jadalyn when teaching about these drugs?
   a. "Full therapeutic effects usually are seen in the first 2 weeks. If not, the dose can be increased."
   b. "Take this medication in the morning to prevent nighttime insomnia."
   c. "Avoid acetaminophen and take ibuprofen or aspirin when needed for pain or fever."
   d. "This can increase your blood pressure, so notify the provider if you have headaches or blurred vision."

2. Based on Jadalyn's family history, which condition would be of most concern with her taking fluoxetine?
   a. Bipolar disorder
   b. Attention deficit hyperactivity disorder
   c. Generalized anxiety disorder
   d. Panic disorder

13.2 Antipsychotics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 13.2.1 Identify the characteristics of drugs used to treat psychosis.
- 13.2.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of drugs used to treat psychosis.
- 13.2.3 Describe nursing implications for drugs used to treat psychosis.
- 13.2.4 Explain the client education related to drugs used to treat psychosis.

Psychosis is a collection of symptoms that include some level of disconnection with reality. These symptoms can include hallucinations, paranoid thoughts, and illogical thinking. Psychosis can be a symptom of a mental illness—most commonly schizophrenia. It can also be a symptom of bipolar disorder or severe depression. Psychotic disorders are generally known to have a strong genetic component. The onset of psychotic symptoms can begin either gradually or quickly. Initial symptoms are commonly seen during adolescence or young adulthood (National Institute of Mental Health [NIMH], 2023c). Psychosis can also develop later in life with neurological conditions such as dementia or be caused by sleep deprivation, certain medications, or alcohol/substance use.

Schizophrenia is a severe mental disorder characterized by disorganized thought processes, blunted or inappropriate emotional responses, and bizarre behavior. In addition, it may involve social withdrawal (**asociality**) by the affected person. Eventually individuals begin to deteriorate and demonstrate a lack of self-care and interpersonal skills. Symptoms of schizophrenia are classified as either positive, referring to an excess of distortion of normal function (e.g., hallucinations), or negative, meaning diminishing or absent behaviors related to motivation

or expression (Correll & Schooler, 2020). Schizophrenia is diagnosed with at least two of the following symptoms present (American Psychiatric Association, 2022). At least one of the symptoms must be delusions, hallucinations, or disorganized speech. Other possible symptoms include disorganized or catatonic behavior (**catatonia**) or negative symptoms (diminished emotional expression or **avolition**). Research suggests that clients with schizophrenia have abnormal neurotransmission systems—primarily the dopaminergic, serotonergic, and glutamatergic systems. It is believed that positive symptoms are associated with overactivity of dopamine$_2$ (D_2) receptors in the basal ganglia, hypothalamus, limbic system, brainstem, and medulla. It is theorized underactive dopamine$_1$ (D_1) receptors in the prefrontal cortex account for the negative symptoms.

SPECIAL CONSIDERATIONS

Schizophrenia in Children

- Schizophrenia in children often presents with more intense clinical manifestations and has a more chronic course.
- The American Academy of Child and Adolescent Psychiatry has established current practice guidelines that advocate for high-quality assessment of the child who is receiving antipsychotics. The purpose of the guidelines is to promote the appropriate use of antipsychotics and to enhance safety. Today, multiple antipsychotics have specific dosing for children and adolescents. These parents' medication guides (https://openstax.org/r/aacap) may be helpful for client education.
- Regulating medication dosing for children is challenging. Children require lower doses to reach full therapeutic effects, yet they also metabolize medications more quickly.

This section of the chapter will focus on treating psychosis. Historically, first-generation or "typical" antipsychotic agents were more effective in managing the positive symptoms versus the negative symptoms; however, the newer second-generation "atypical" medications have shown effectiveness in treating both the positive and negative symptoms. Antipsychotics are targeted at thought processes rather than affective states. Although they are not a cure, they can help both adult and pediatric clients be able to adequately function in a healthier manner. In acute psychosis, the goal is to reduce symptoms in the first week and normalize clients' eating and sleeping patterns. Subsequent goals are to increase the ability for self-care and increase socialization. Most of these drugs take 1–2 months to reach full therapeutic effects. With adequate drug treatment, clients can engage in individual or group psychotherapy sessions as well as return to their level of functioning prior to the illness.

SAFETY ALERT

Beers Criteria®

The Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults is a list published by the American Geriatrics Society describing medications that are potentially harmful if prescribed to clients older than 65 years. Antipsychotics are included on the list because they are linked to higher rates of cognitive decline and death in persons with dementia.

(Source: American Geriatrics Society, 2023)

CLINICAL TIP

Antipsychotics

First-generation antipsychotics are frequently referred to as "neuroleptics" because of the increased risk of producing extrapyramidal neurologic effects, including **pseudoparkinsonism**, **dystonia** (spasms of the tongue, back, legs, and neck), **akathisia** (not being able to sit still), and **tardive dyskinesia** (abnormal muscle movements). Health care providers should monitor clients for extrapyramidal effects so they can be treated and the antipsychotic medication can be changed (Ameer & Saadabadi, 2023).

Antipsychotics fit into the classification of dopamine receptor antagonists (blockers). They are used to treat

disorders that involve thought processes. They help clients with organizing their thoughts and responding appropriately to stimuli. The therapeutic effects are most likely due to blocking dopamine receptors. Unfortunately, these medications can also bind to a variety of receptors, which leads to many of the ADRs. Antipsychotics are categorized in two main classes: first-generation agents, also known as typical or conventional, and second-generation agents, also known as atypical. These categories are based on their mechanism of action (described in the following sections). Although their names may imply that psychosis is the only condition these drugs are used for, there are numerous psychiatric disorders for which these drugs can be useful.

Clients should be made aware they will usually need to remain on these drugs for years, if not for life, because there is a high rate of relapse when drug therapy is stopped. Most antipsychotics come in an oral form. Those clients who are unable or unwilling to take daily doses may receive periodic injections of a long-acting form (LAIs). The benefit of the LAIs is that they allow prescribers to tailor pharmacotherapy to each client's needs. The LAIs are administered via **depot injections**. This refers to the way the drug is deposited and stored in the muscle before being absorbed. Because the drug takes a longer time to move out of the muscle and into the bloodstream, its action is prolonged.

First-Generation (Typical) Antipsychotics

First-generation antipsychotics are classified by their potency (strength). The level of potency (low, medium, or high) refers to the concentration of the drug needed to produce a given response. Keep in mind that this is different from efficacy. All first-generation agents have the same ability to relieve symptoms of psychosis (efficacy). In addition to blocking dopamine receptors, they also block muscarinic, histaminergic, and alpha-adrenergic receptors, leading to numerous adverse effects (discussed later in this chapter). The three most common first-generation antipsychotics are:

- *Chlorpromazine:* This is a low-potency agent and a phenothiazine. It is also used to decrease preoperative restlessness and apprehension, treat intermittent porphyria, as an adjunct in the treatment of tetanus, and to help control nausea, vomiting, and intractable hiccups.
- *Fluphenazine:* This is a high-potency agent and a phenothiazine. Compared to other antipsychotics, this drug has a low potential for causing anticholinergic effects. It is available in oral and intramuscular forms.
- *Haloperidol:* This is a high-potency nonphenothiazine. It is frequently used to treat acute psychiatric situations when it is given intramuscularly. Its mechanism of action, ADRs, and contraindications are the same as for chlorpromazine. An added contraindication is severe mental depression.

Table 13.12 lists common first-generation antipsychotics and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Chlorpromazine (Thorazine)	*Adults (mild to moderate symptoms):* Initial dose: 25 mg 3 times daily; increase gradually until effective dose is reached, usually 400 mg/day. *Adults (severe symptoms):* Initial dose: 25 mg 3 times daily; after 1–2 days, daily dosage may be increased by 20–50 mg until client becomes calm. *Older adults:* Initial dose: 1/4 to 1/3 of the level for younger adults. *Children (6 months to 12 years for severe behavioral problems):* Outpatient dose: 0.25 mg/lb orally every 4–6 hours as needed. Inpatient dose: 50–200 mg/day orally until symptoms improve.
Fluphenazine (Prolixin, Modecate)	*Adults:* Initial dose: 2.5–10 mg orally divided into intervals of 6–8 hours. Maximum dose: 40 mg/day; maintenance dose: 1–5 mg/day as a single dose.
Haloperidol (Haldol)	*Oral:* *Adults:* 0.5–5 mg orally 2 or 3 times daily. *Children (3–12 years):* Initial dose: 0.5 mg/day orally. Increase dose by 0.5 mg increments at intervals of 5–7 days until desired effect is achieved. *Intramuscular:* *Adults:* *Long-acting:* Starting dose form should be based on 10–20 times the previous daily dose in oral haloperidol equivalents and adjusted as needed. *Short-acting:* 2–5 mg as often as every hour up to a maximum dose of 20 mg/day.

TABLE 13.12 **Drug Emphasis Table: First-Generation Antipsychotics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Most of the ADRs are related to these drugs' anticholinergic properties, including blurred vision, dry mouth, constipation, urine retention, nasal congestion, and photophobia. Arrhythmias can be caused by the dopamine-blocking effects or prolongation of the QTc interval, which could lead to fatal arrhythmias. Prolactin levels will increase, causing gynecomastia and changes in libido. First-generation antipsychotics are known to cause **extrapyramidal symptoms** (EPS), which are involuntary, uncontrollable movements. These include pseudoparkinsonism (muscle tremors, cogwheel rigidity, stiff facial muscles, drooling due to difficulty swallowing, shuffling gait, and slow movements), dystonia, akathisia, and tardive dyskinesia. Extrapyramidal symptoms may be more problematic with depot injections.

Neuroleptic malignant syndrome (NMS) is a rare but potentially fatal condition that can develop with antipsychotic use. The clinical manifestations include a sudden high-grade fever, fluctuations in blood pressure, dysrhythmias, extreme muscle rigidity, and significant tachycardia. Immediate supportive management must be instituted if this develops, which might include cooling blankets/fluids and administering antipyretics (drugs to reduce fever), antiarrhythmics, and dantrolene to treat muscle rigidity.

The manifestations of Parkinson's disease can be exacerbated by antipsychotics due to their effect on dopamine receptors. This can happen with any antipsychotic that causes EPS. In addition, these drugs can cause urinary retention and constipation. Individuals who have a mechanical or neurological obstruction of the renal or GI system should avoid these drugs, including those with benign prostatic hyperplasia (BPH).

Due to their anticholinergic properties, these drugs can increase intraocular pressure, worsening glaucoma and possibly causing vision loss. Furthermore, those with a seizure disorder may need an increase in their antiseizure medications because the antipsychotics tend to lower the seizure threshold.

Alcohol intake and taking medications that cause CNS depression will amplify the depressant effect.

SAFETY ALERT

Similarly Named Drugs Associated with First-Generation Antipsychotics

Do not confuse chlorpromazine (antipsychotic) with chlordiazepoxide (sedative) or chlorpropamide (sulfonylurea

antidiabetic).

(Source: ISMP, 2023)

Table 13.13 is a drug prototype table for first-generation antipsychotics featuring haloperidol. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class First-generation antipsychotic (typical antipsychotic) **Mechanism of Action** Blocks dopamine-2 receptors, which prevents the stimulation of the postsynaptic neurons by dopamine Exact mechanism of action for schizophrenia is unclear	**Drug Dosage** *Oral:* *Adults:* 0.5–5 mg orally 2 or 3 times daily. *Children (3–12 years):* Initial dose: 0.5 mg/day orally. Increase dose by 0.5 mg increments at intervals of 5–7 days until desired effect is achieved. *Intramuscular:* *Adults:* *Long-acting:* Starting dose form should be based on 10–20 times the previous daily dose in oral haloperidol equivalents and adjusted as needed. *Short-acting:* 2–5 mg as often as every hour up to a maximum dose of 20 mg/day.
Indications Schizophrenia Treatment of psychotic symptoms associated with brain impairment (head trauma, tumor, stroke, alcohol withdrawal, and overdoses of CNS stimulants) **Therapeutic Effects** Blocks dopamine receptors in the brain Limits the stimuli coming into the brain	**Drug Interactions** CNS depressants, such as opioids or sedatives Antiarrhythmic medications that prolong the QTc interval **Food Interactions** Kava kava Alcohol
Adverse Effects Prolongation of the PR and QTc interval Anticholinergic effects (blurred vision, **xerostomia**, constipation, urine retention, nasal congestion, photophobia) Sexual dysfunction Hypotension/arrhythmias Pseudoparkinsonism Akathisia Tardive dyskinesia Sedation/drowsiness Impaired mobility Impaired speech and mental processes	**Contraindications** Parkinson's disease Older adults with dementia Cardiac arrhythmias/prolonged QTc interval Liver damage Coronary artery disease (CAD) Cerebrovascular disease Caution: Glaucoma Seizures Active alcohol use disorder

TABLE 13.13 **Drug Prototype Table: Haloperidol** (source: https://dailymed.nlm.nih.gov/dailymed/)

Second-Generation (Atypical) Antipsychotics

The second-generation antipsychotics, also known as atypical antipsychotics, are the drugs of choice. This is especially true for clients who are newly diagnosed. The atypical antipsychotics block both dopamine and serotonin receptors. This class of antipsychotics has a broader range of action than the first-generation agents because of their effects on the serotonergic, noradrenergic, and dopaminergic systems. They seem to be more effective in relieving some symptoms and usually produce milder adverse effects (Ameer & Sadabadi, 2023). The most common second-generation antipsychotics are:

- *Aripiprazole:* This is the first of a new class of atypical antipsychotic medications called the *dopamine system*

stabilizers. This class is sometimes referred to as a third-generation antipsychotic. In its oral form, aripiprazole can be used in the management of schizophrenia, major depressive disorder, bipolar disorder, irritability related to autism spectrum disorder, and Tourette syndrome. In its injectable, immediate-release form, it is used to treat agitation associated with schizophrenia or bipolar mania. This drug does not prolong the QTc interval; however, the FDA has issued a safety alert, confirming that compulsive or uncontrollable urges to gamble, binge eat, shop, and have sex with multiple partners have been reported.

- *Cariprazine:* Used to treat schizophrenia or mania and depression related to bipolar disorder. It is also used to treat MDD.
- *Clozapine:* This medication was one of the first atypical antipsychotic medications used to treat schizophrenia, but because of its side effects, is only used when other treatments have failed. Clozapine is available only through to the FDA's Approved Risk Evaluation and Mitigation Strategies (REMS) program to ensure monitoring of WBC count and absolute neutrophil count.
- *Lurasidone:* Used to treat schizophrenia and bipolar depression in clients age 13 and older. Administering this drug with food can greatly increase its absorption. This drug does not prolong the QTc interval, cause orthostatic hypotension, or have any cholinergic effects.
- *Olanzapine:* In addition to treating schizophrenia, this drug is used for manic or mixed episodes of bipolar disorder and can be given parenterally to treat acute agitation.
- *Paliperidone:* Used in clients age 12 and over to treat schizoaffective disorders. This is a major active metabolite of risperidone; therefore, it has the same therapeutic and adverse effect profiles. Paliperidone is available in three forms: one short-acting oral and two long-acting injectables (one administered monthly and the other every 3 months).
- *Quetiapine:* Used to treat schizophrenia and depressive disorder as well as for short-term treatment of acute manic episodes associated with bipolar disorder. The extended-release form is for use only in adults.
- *Risperidone:* Used to treat schizophrenia and acute bipolar mania. It is also frequently used to manage irritability and aggression associated with autism spectrum disorder in children and adolescents. In schizophrenia, relief of positive and negative symptoms can occur in as little as 1 week.
- *Ziprasidone:* Indicated for schizophrenia and bipolar disorder.

Table 13.14 lists common second-generation antipsychotics and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Aripiprazole (Abilify)	*Adults:* 10–15 mg/day orally initial dose; effective dose range: 10–30 mg/day. *Adolescents (13–17 years):* Initial dose: 2 mg/day orally; target dose: 10 mg /day.
Cariprazine (Vraylar)	*Adults:* 1.5 mg orally daily; recommended dose: 1.5–6 mg/day. Pediatric safety, effectiveness, and dose have not been established.
Clozapine (Clozaril)	*Adults:* Initial dose: 12.5 mg/day orally; total daily dose can be increased in increments of 25–50 mg/day; target dose: 300–450 mg/day in divided doses.
Lurasidone (Latuda)	*Adults and adolescents (13–17 years):* Initial dose: 20 mg/day orally. Maximum dose for adults: 120 mg/day. Maximum dose for adolescents: 80 mg/day.
Olanzapine (Zyprexa)	*Adults:* 5–10 mg/day orally; target dose: 10 mg/day. *Adolescents (13-17 years):* Initial dose: 2.5–5 mg/day; target dose: 10 mg/day.
Paliperidone (Invega)	*Adults:* Initial dose: 6 mg/day orally; maximum dose: 12 mg/day. *Adolescents (12–17 years):* 3 mg orally once daily. Maximum dose: 6 mg for clients weighing less than 51 kg; 12 mg for clients weighing 51 kg or greater.
Quetiapine (Seroquel)	*Adults:* Initial dose: 300 mg/day orally titrated to effect; maximum dose 800 mg/day. *Adolescents:* Initial dose: 50 mg/day orally; titrated to effect: maximum 800 mg/day.
Risperidone (Risperdal)	*Adults:* 2 mg/day orally; effective dose: 4–16 mg/day. *Adolescents:* Initial dose: 0.5 mg/day; effective dose: 1–6 mg/day.
Ziprasidone (Geodon)	*Adults:* 20 mg orally twice daily; maximum dose: 80 mg twice daily for schizophrenia; 40 mg orally twice daily; 80 mg twice daily for bipolar disorder.

TABLE 13.14 Drug Emphasis Table: Second-Generation Antipsychotics (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

For second-generation antipsychotics, the risk of seizures is higher as the drug dose increases. Hematologic effects include agranulocytosis, neutropenia, and fatal agranulocytosis. Clozapine is subject to additional monitoring through the FDA's REMS program to decrease the risk of severe neutropenia. Metabolic effects are more common with these medications and include hyperglycemia and weight gain. Concerning ADRs for quetiapine include increased systolic and diastolic readings, decreased high-density cholesterol, and increased total cholesterol, low-density cholesterol, and triglycerides.

Drugs with anticholinergic properties will potentiate these effects of clozapine. Alcohol can increase the sedative effect. Cimetidine and caffeine can increase the risk of toxicity for clozapine.

SAFETY ALERT

Similarly Named Drugs Associated with Second-Generation Antipsychotics

Do not confuse:

- Aripiprazole (antipsychotic) with pantoprazole (proton pump inhibitor)
- Clozaril (antipsychotic) with Colazal (anti-inflammatory for inflammatory bowel disorder)
- Olanzapine (antipsychotic) with quetiapine (antipsychotic)
- Zyprexa (antipsychotic) with Zestril (ACE inhibitor) or Zyrtec (histamine-1 receptor antagonist)
- Risperdal (antipsychotic) with Restoril (benzodiazepine sedative-hypnotic) or Ropinirole (dopamine agonist)

(Source: ISMP, 2023)

Table 13.15 is a drug prototype table for second-generation antipsychotics featuring risperidone. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Second-generation antipsychotic (atypical antipsychotic) **Mechanism of Action** Blocks dopamine and serotonin receptors in the brain	**Drug Dosage** *Adults:* 2 mg/day orally; effective dose: 4–16 mg/day. *Adolescents:* Initial dose: 0.5 mg/day; effective dose: 1–6 mg/day.
Indications Schizophrenia Bipolar mania **Therapeutic Effects** Decreases hallucinations and disordered thoughts in clients with schizophrenia Decreases symptoms of mania including irritability, aggressive thoughts, elevated mood and activity, and sexual interest	**Drug Interactions** Carbamazepine Cimetidine Ranitidine Fluoxetine Paroxetine Erythromycin Amitriptyline **Food Interactions** Alcohol
Adverse Effects Orthostatic hypotension Increased risk of seizures Hematologic effects (leukopenia, neutropenia, and agranulocytosis) Hyperglycemia Dyslipidemia Neuroleptic malignant syndrome Development of diabetes mellitus Weight gain	**Contraindications** Known hypersensitivity to risperidone, paliperidone, or any derivatives Dementia-related psychosis Caution: Severe renal impairment Hepatic impairment Cardiovascular disease Diabetes mellitus Pulmonary disease

TABLE 13.15 **Drug Prototype Table: Risperidone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antipsychotics:

- Watch carefully for developmental progress in children.
- Monitor for symptoms of schizophrenia.
- Obtain baseline physical assessment and relevant tests including an electrocardiogram, CBC, electrolytes, liver and renal function tests, lipid panel, blood glucose levels, and thyroid function. Continue to monitor these on an ongoing basis to identify potential adverse effects.
- Obtain baseline vital signs and urinary output.
- Monitor weight for weight gain, agitation, and/or sleep disturbances.
- Evaluate for the potential effects of hyperprolactinemia (high levels of the hormone prolactin in the blood).
- Assess for any anticholinergic effects. Promote comfort measures if necessary, such as laxatives or catheterization.
- Measure the PR and QTc interval at baseline and during the use of thioridazine or ziprasidone.
- Obtain a detailed history for any cardiovascular conditions, glaucoma, diabetes, obstructions, seizure disorder, pregnancy (or thinking about getting pregnant), and breastfeeding.
- Ensure the client is not a danger to themselves or others.
- Auscultate bowel sounds every 4 hours if client is an inpatient. The constipation caused by clozapine is significant and can progress to intestinal ischemia and necrotizing colitis.
- To prevent any unnecessary stress, explain gynecomastia and the reason it occurs.
- Assess CNS alertness and orientation and provide safety precautions when necessary.
- Assess for any extrapyramidal effects and provide safety measures.
- Ensure client receives an annual eye exam to monitor for glaucoma or worsening of glaucoma.
- Care for the client in a holistic manner, such as proper nutrition, adequate hygiene, activity level, and social

interactions.
- With acute psychotic episodes, observe for decreased agitation, combativeness, and psychomotor activity to evaluate therapeutic effectiveness.
- Observe for decreased psychotic behaviors, such as decreased hallucinations and delusions.
- Ensure clozapine does not get stopped abruptly because it will cause acute psychosis. This drug should be tapered over a 2-week period.
- For clients taking clozapine, perform a thorough assessment of their cardiovascular and cardiopulmonary status.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antipsychotic should:

- Drink adequate amounts of water (at least 64 ounces/day or other prescribed amount), especially during hot weather.
- Have a total understanding that full therapeutic effects will not occur immediately; it may take several weeks to be able to experience effects.
- Obtain weekly blood tests to determine safe and effective dosage.
- Lie down for 30–60 minutes after an IM injection to prevent hypotension.
- Take the oral form 1–2 hours prior to bedtime because the drug peaks in 2 hours.
- Wear protective clothing when out in the sun.
- Report dark urine, right upper quadrant pain, clay-colored stools, and yellowing of the eyes or skin to the provider.
- Notify the health care provider if sore throat, fever, or flu-like symptoms arise.
- If needed, take the drug with food to decrease gastric upset.
- Increase fluid intake, dietary fiber, and exercise to prevent constipation.
- Be aware that only 1 week of medicine will be dispensed at a time (clozapine).
- Immediately notify the provider if having difficulty moving their bowels. The provider may need to prescribe a stool softener.
- Practice frequent hand hygiene and wear a mask in public if white blood cell count is low to decrease risk of infection.
- Practice good oral care and rinse mouth frequently or chew on sugarless gum to manage symptoms of dry mouth.
- Monitor for extrapyramidal symptoms and notify the provider if they occur.

The client taking an antipsychotic *should not:*

- Allow the liquid concentrations to touch the skin because it can cause contact dermatitis.
- Quickly change positions due to orthostatic hypotension.
- Drive a vehicle or operate heavy machinery due to dizziness and sedation.

FDA BLACK BOX WARNING

Antipsychotics

First- and second-generation antipsychotics: Increasing mortality occurs in the older adult with dementia-related psychosis.

Aripiprazole: Use places the client at risk for developing compulsive or uncontrollable urges to gamble, shop, binge eat, or be promiscuous.

13.3 Mood Stabilizers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 13.3.1 Identify the characteristics of drugs used to treat bipolar disorder.
- 13.3.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of drugs used to treat bipolar disorder.
- 13.3.3 Describe nursing implications for drugs used to treat bipolar disorder.
- 13.3.4 Explain the client education related to drugs used to treat bipolar disorder.

Bipolar disorder is a complex brain-based illness with a primary characteristic of mood disturbance. Clients alternate between episodes of depression and mania. Depression was described in the beginning of this chapter. Mania involves a period of abnormally and persistently elevated or irritable mood and increased goal-directed activity or energy (American Psychiatric Association, 2022). During this period, at least three of the following symptoms are present: grandiosity, decreased need for sleep, more talkative, flight of ideas or racing thoughts, distractibility, increased activity or agitation, and excessive involvement in risky behaviors.

Most times, clients seek help when they are in the depressed stage. However, if a client has an undiagnosed bipolar disorder, putting them solely on an antidepressant can cause the client to experience one or more manic phases. There are two main subtypes of this disorder. Bipolar Type 1 is characterized by the occurrence of one or more manic episodes interspersed with major depression. Bipolar Type 2 is characterized by occurrence of one or more major depressive episodes accompanied by at least one manic or hypomanic episode (persistent irritability without euphoria) (NIMH, 2023a).

Lithium

Lithium is a naturally occurring metallic salt. It is used mainly to treat and prevent mania. It has historically been the "gold standard" mood stabilizer, effectively controlling manic episodes as well as decreasing the frequency and intensity of manic cycles (Volkmann et al., 2020). Lithium has a narrow margin of safety; even small increases in the dose could be toxic (Hedya et al., 2023). The goal is to initially maintain the serum lithium level between 0.6 and 1.2 mEq/L (Coryell, 2022). Target maintenance drug levels are closer to 0.6 mEq/L. Table 13.16 describes levels of lithium toxicity.

Serum Drug Levels	Clinical Manifestations
1.5–2.5 mEq/L	Lethargy, tremors, nausea, and vomiting
2.5–3.5 mEq/L	Confusion, agitation, delirium, tachycardia, and hypertonia
>3.5 mEq/L	Coma, seizures, hyperthermia, and hypotension

TABLE 13.16 Adverse Reactions Related to Serum Levels of Lithium (source: Hedya et al., 2023)

Adverse Effects and Contraindications

Lithium is excreted through the kidneys unchanged; therefore, adequate renal function is essential. Because lithium is tied to sodium resorption, any drug that affects sodium balance may alter lithium concentrations, leading to either treatment failure or toxicity. Examples include diuretics, NSAIDs, and angiotensin-converting enzyme (ACE) inhibitors. Lithium interacts with other medications including carbamazepine (CNS toxicity), neuromuscular blocking agents (prolonged effects), and other serotonergic drugs (serotonin syndrome). Addison's disease is a contraindication because the person is losing more sodium through the kidneys due to the lack of aldosterone. The kidneys then will reabsorb lithium back into the bloodstream, which can quickly cause lithium toxicity. Lithium inhibits the synthesis and release of thyroid hormones, resulting in hypothyroidism. Theophylline increases the renal excretion of lithium, resulting in subtherapeutic effects.

Table 13.17 is a drug prototype table for mood stabilizers featuring lithium. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Mood stabilizer **Mechanism of Action** Affects the synthesis, release, and reuptake of acetylcholine, dopamine, GABA, and norepinephrine within the brain Stabilizes postsynaptic receptor sensitivity to neurotransmitters Has a neuroprotective effect on areas of the brain associated with mood by stimulating neuronal growth The exact mechanism of action is unknown	**Drug Dosage** *Immediate release (acute manic episodes):* *Adults:* 300 mg orally 3 times daily; usual dose: 900–1800 mg/day orally in 3–4 divided doses. *Extended release (maintenance dosage):* *Adults:* 450 mg orally twice daily. Usual dose: 900–1800 mg/day orally in 2 divided doses. *Children >12 years:* 450 mg orally twice daily. Maintenance dose: 15–60 mg/kg/day orally 3 times daily.
Indications Treatment of active manic episodes Maintenance therapy to prevent or diminish the frequency and intensity of future manic episodes **Therapeutic Effects** Alters the sodium transport of nerve and muscle cells Inhibits the release of NE and dopamine from stimulated neurons Increases the intraneuronal stores of NE and dopamine Decreases intraneuronal content of second messengers, which allows it to selectively modulate the responsiveness of the hyperactive neurons	**Drug Interactions** Diuretics Serotonergic agent Neuromuscular blocking agents Carbamazepine Lithium-iodide salt combination Theophylline **Food Interactions** Sodium intake Deficit fluid intake
Adverse Effects Nephrotoxic Neurotoxic Toxic to the thyroid gland (goiter) Weight gain Metallic taste Hand tremors Polyuria/polydipsia Nausea Vomiting Diarrhea Edema/weight gain Muscular weakness	**Contraindications** Renal failure Cardiovascular insufficiency Addison's disease Untreated hypothyroidism Children <12 years of age Pregnancy and breastfeeding Caution: Vomiting/diarrhea Increase or decrease of sodium intake Diaphoresis/dehydration Suicidal or impulsive clients Active infection with fever

TABLE 13.17 **Drug Prototype Table: Lithium** (source: https://dailymed.nlm.nih.gov/dailymed/)

CLINICAL TIP

Atypical Antipsychotic for Bipolar Disorder

In December 2021, the FDA approved lumateperone (Caplyta) for bipolar depression. The drug is an atypical antipsychotic. It can be used as a monotherapy or in combination with lithium or valproate. It is available as a once-daily oral pill that needs no dose changes.

Antiseizure Medications

Selected antiseizure medications can be used to treat mood disorders, usually in combination with other medications. Please refer to Anticonvulsant Drugs and Drugs to Treat Epilepsy, Migraine Headaches, and

Intracranial Emergencies for a more detailed discussion of antiseizure medications.

Table 13.18 lists common antiseizure medications and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Carbamazepine (Tegretol)	*Adults and children >12 years:* Initial dose: 200 mg orally twice daily (tablet); may increase by up to 200 mg/day in divided doses on a weekly basis. Maximum dose: 1200 mg in adults and 1000 mg in children 12–15 years. Therapeutic range: 4–12 mg/L.
Lamotrigine (Lamictal, Subvenite)	*Monotherapy:* First 2 weeks, 25 mg/day orally; week 3, increase to 50 mg/day; week 5, increase to 100 mg/day; week 6, increase to 200 mg/day (maximum). *As an adjunct to valproic acid:* First 2 weeks, 25 mg orally every other day; week 3, increase to 25 mg/day; week 5, increase to 50 mg/day; week 6, increase to 100 mg/day. Therapeutic range: 3–14 mcg/mL (or titrated to therapeutic effect).
Valproic acid, divalproex sodium (Depakote, Depakote ER)	*Acute mania in adults:* Initial dose: 250–500 mg 3 times daily; increase dose rapidly. Maximum dose: 60 mg/kg/day. *Less acute mania in adults:* Initial dose: 200–500 mg; titrate upward as tolerated. Therapeutic range: 50–125 mcg/mL.

TABLE 13.18 **Drug Emphasis Table: Antiseizure Medications** (source: https://dailymed.nlm.nih.gov/dailymed/; Betchel et al., 2023; Rahman et al., 2023)

Nursing Implications

The nurse should do the following for clients who are taking mood stabilizers:

- Obtain baseline and periodic lab work including serum carbamazepine levels or serum lithium levels if indicated, CBC with differential, electrolytes, liver function tests, and thyroid-stimulating hormone (TSH) levels.
- Evaluate client's medical history and ensure there are no renal or cardiac concerns. Obtain a baseline electrocardiogram.
- Assess for any indication of suicidal ideations. Institute suicide precautions for at-risk clients.
- Monitor temperature, heart rate/rhythm, respiratory status, and blood pressure periodically.
- Assess orientation, affect, reflexes, bowel sounds, amount of urine output, and lung sounds.
- Monitor client's renal function while on lithium.
- If CNS effects occur, provide safety measures to prevent client injury.
- Monitor for decreased manic behavior and impulsivity.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a mood stabilizer should:

- Contact the health care provider with the first signs of rash if taking carbamazepine or lamotrigine.
- Notify the health care provider with unusual and easy bruising, blood in the urine or stool, fever, sore throat, right upper quadrant pain, and jaundice.
- Consider an additional or alternate form of contraception because carbamazepine decreases the effectiveness of certain hormonal contraceptives.
- Drink 8–12 glasses of water daily to prevent dehydration, which could cause lithium toxicity. Also, maintain a consistent sodium intake.
- Be aware they can take lithium with food if they experience gastric irritation.
- Continue taking the medication as prescribed despite their symptoms subsiding because this type of therapy is long term.
- Notify the health care provider and stop taking the drug immediately if manifestations of overdose occur (vomiting, diarrhea, ataxia, tremor, drowsiness, and muscle weakness).
- Notify the health care provider if thinking about getting pregnant. Studies have shown that lithium can be

harmful to the fetus.
- Follow the prescribed schedule for lab work to check appropriate serum drug levels.

The client taking a mood stabilizer *should not:*

- Spend time in the sun without sunscreen and other coverings.
- Drive or perform tasks requiring alertness and coordination until effects of carbamazepine are known.
- Increase their exercise routine during hot weather because this can increase the risk of dehydration and lithium toxicity.
- Abruptly stop lithium, to avoid negative manifestations.
- Take the morning dose of lithium until a blood sample has been obtained. (Blood should be drawn about 12 hours after the last lithium dose.)
- Alter dietary salt intake. If decreased, lithium toxicity can result. If increased, lithium will be subtherapeutic.

13.4 Anxiolytics and Sedative-Hypnotics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 13.4.1 Identify the characteristics of drugs used to treat anxiety and sleep disorders.
- 13.4.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of drugs used to treat anxiety and sleep disorders.
- 13.4.3 Describe nursing implications for drugs used to treat anxiety and sleep disorders.
- 13.4.4 Explain the client education related to drugs used to treat anxiety and sleep disorders.

Anxiety can be described as a feeling of nervousness, apprehension, and/or worry about a future threat. Anxiety disorders involve excessive fear and anxiety and corresponding behaviors (American Psychiatric Association, 2022). Generalized anxiety disorder (GAD), panic disorder, obsessive-compulsive disorder (OCD), social anxiety disorder, and post-traumatic stress disorder (PTSD) are examples of anxiety disorders. Anxiety is considered pathological if it is (1) disproportionate to events, (2) sustained over a significant time period, (3) significantly impairing function during usual activities of daily living, and (4) apparently unrelated to any identifiable event or situation. Pathological levels of anxiety require treatment and usually will not fully resolve without therapeutic intervention. Clinical manifestations of anxiety are related to the activation of the sympathetic nervous system response. These include muscle tension, restless feeling, trembling, difficulty concentrating, irritability, tachycardia, palpitations, diaphoresis, dry mouth, dyspnea, and dizziness. Untreated high levels of anxiety predispose people to other comorbidities, such as hypertension, substance use, or depression. These high levels can impair memory, perception, judgment, and motor responses.

A simplistic explanation related to the pathophysiology of anxiety involves an excess of excitatory neurotransmitters (norepinephrine) or a deficiency of inhibitory neurotransmitters (GABA). Most of the medications known to improve symptoms of anxiety act directly or indirectly on the GABA system. Benzodiazepines are widely used for short-term treatment until the prescribed antidepressant reaches therapeutic levels. (Antidepressants were discussed earlier in the chapter.)

Sleep is essential for body restoration. During sleep, tissue repair, synthesis of skeletal muscle protein, and secretion of growth hormone occur. Insomnia is the inability to obtain an adequate amount of sleep needed to function efficiently during the day. Insomnia may be situational, lasting a few days to a few weeks. Insomnia disorder, however, is defined as a significant inability to initiate sleep (**sleep latency**) or maintain sleep, or early morning awakening with the inability to return to sleep (American Psychiatric Association, 2022). The occurrence is at least 3 nights/week and is present for at least 1 month and may persist for longer than 3 months. Insomnia disorder leads to increased morbidity (such as psychosis) and mortality. Many clients with insomnia have high rates of depression and anxiety.

Drug therapy includes benzodiazepines and the nonbenzodiazepine sedatives. **Anxiolytics** (antianxiety drugs) and **sedative-hypnotics** (drugs to invoke relaxation and produce sleep) are CNS depressants that have similar effects. The difference between the effects depends largely on the dose. Large doses of antianxiety and sedative-hypnotic

agents produce sleep, and small doses of sedative-hypnotics have anxiolytic or sedative effects.

Benzodiazepines

Benzodiazepines are usually prescribed on a short-term basis for disabling anxiety and are considered second-line therapy due to the risk of dependence. They quickly reduce or prevent anxiety without causing extreme sedation. Benzodiazepines are classified as a Schedule IV controlled substance due to their potential for misuse and physical dependency. Benzodiazepines work in the limbic system and the reticular activating system (RAS) to make GABA more effective. GABA stabilizes the postsynaptic cells, which results in the interference of neuron firing.

When treating anxiety, a lower dose is necessary compared to when using it for sedative purposes. In addition to anxiety, these medications can be used for alcohol withdrawal, agitation, and seizure disorders. These drugs must be tapered slowly when discontinuing them or the client will experience withdrawal symptoms.

SAFETY ALERT

Reversal Agent for Benzodiazepine Toxicity

Flumazenil is a specific benzodiazepine receptor antagonist and is beneficial in reversing the effects of benzodiazepine. It should be available for use as needed to reverse the effects of benzodiazepines administered for sedation. It is also used emergently to treat benzodiazepine overdose.

(Source: Shoar et al., 2023)

The most commonly used benzodiazepines are:

- *Diazepam:* Children are more sensitive to diazepam, especially related to mood and/or mental changes. They may experience **paradoxical medication effects** of CNS stimulation and excitation instead of getting a calming effect. Older adults are more sensitive to diazepam's effects of drowsiness and poor coordination.
- *Alprazolam:* This drug is preferred over diazepam due to its rapid onset of action.
- *Clonazepam:* Monitor for suicidal ideations, liver function, and CBC.
- *Lorazepam:* This drug is most likely the benzodiazepine of first choice. It provides rapid tranquilization of agitated clients. When administered IV, it can induce procedural amnesia. When administered orally, it can help combat anxiety disorders and depression-associated anxiety along with stress-related insomnia.
- *Midazolam:* This drug is a short-acting medication. It is commonly used prior to surgery or procedures. It can be continuously administered via IV to maintain sedation. In addition, it is considered a valuable adjunct in pediatric anesthesia because it comes in an oral flavored syrup.
- *Temazepam:* This is the drug of choice for older adults and those with liver disease.
- *Triazolam:* This drug has a very rapid onset of action. It should be administered while the client is in bed. Cirrhosis of the liver and hepatic insufficiency are contraindications for this drug.

Table 13.19 lists common benzodiazepines and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Diazepam (Valium)	*Adults:* 2–10 mg orally 2–4 times daily; 5–10 mg intramuscularly or intravenously or 0.2 mg/kg by rectum. *Older or debilitated adults:* 2–5 mg orally 1–2 times/day. *Children ≥6 months:* 0.12–0.8 mg/kg/day orally in divided doses every 6–8 hours.
Alprazolam (Xanax)	*Anxiety:* *Adults:* Immediate release: 0.25–0.5 mg orally 3 times daily. Average maintenance dose: 1–4 mg/day. Maximum dose: 4 mg/day in divided doses. *Older or debilitated adults:* 0.25 mg orally 2–3 times/day. *Panic Disorder:* *Adults:* *Immediate release:* Initial dose: 0.5 mg orally 3 times daily. Gradually increase to 4–10 mg/day. *Extended release:* Initial dose: 0.5–1 mg/day orally. Gradually increase as needed. Maximum dose: 3–6 mg/day. *Children:* Dosage has not been established for those under age 18.
Clonazepam (Klonopin)	*Panic Disorder:* *Adults and children >10 years:* Initial dose: 0.25 mg orally twice daily. May increase dose to 1 mg daily after 3 days. Maximum dose: 4 mg/day.
Lorazepam (Ativan)	*Adults:* 2–6 mg/day orally in 2–3 divided doses. Maximum dose: 10 mg/day. *Children:* Safety and effectiveness have not been established for those under age 12.
Temazepam (Restoril)	*Adults:* Average range: 7.5–30 mg/day before bedtime. *Children:* Safety and effectiveness have not been established for those under age 12.
Triazolam (Halcion)	*Adults:* Recommended dose: 0.25 mg once nightly before bedtime. Maximum dose: 0.5 mg once nightly. *Children:* Safety and effectiveness have not been established for those under age 12.

TABLE 13.19 Drug Emphasis Table: Benzodiazepines (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Due to the prolonged half-life, both therapeutic and adverse effects are more likely to occur after 3 days of therapy. A client with a history of psychosis should avoid taking benzodiazepines due to the potential exacerbation of symptoms. Acute narrow-angle glaucoma is also a contraindication because this drug class can increase the intraocular pressure. Acute alcohol intoxication or opioid use can intensify the CNS depressant effects. Anyone who is pregnant or breastfeeding should avoid these drugs because they can easily cross the placenta and mammary glands, causing significant sedation in the fetus or infant. Benzodiazepines may produce paradoxical excitement and aggression in adults older than age 50 who have a history of psychosis. Likewise, clients with impaired hepatic function should avoid taking these medications because they are metabolized by the liver. Clients with renal impairment should avoid this drug because the active metabolites may accumulate, resulting in excessive sedation and respiratory depression. Calcium channel blockers decrease the benzodiazepine's drug metabolism, leading to increased adverse drug effects. Cimetidine is a hepatic enzyme inhibitor. If the dose of the sedative-hypnotic is not decreased, it will accumulate and become toxic. Taking disulfiram concurrently can potentiate the effects of benzodiazepines.

! SAFETY ALERT

Similarly Named Drugs Associated with Benzodiazepines

Do not confuse:

- Diazepam (benzodiazepine) with diltiazem (Calcium channel blocker)
- Alprazolam (benzodiazepine) with clonazepam or lorazepam (both benzodiazepines)
- Xanax (benzodiazepine) with Tenex (CNS nonstimulant)
- Clonazepam (benzodiazepine) with clozapine (antipsychotic)
- Klonopin (benzodiazepine) with clonidine (alpha-2 adrenergic agonist)

- Lorazepam (benzodiazepine) with Lovaza (omega-3 acid ethyl esters)

(Source: ISMP, 2023)

SPECIAL CONSIDERATIONS

Age

- *Children:* Great caution needs to be given when administering benzodiazepines or sedative-hypnotics to children because their response to the drug is very unpredictable. Of the benzodiazepines, only chlordiazepoxide, clonazepam, lorazepam, midazolam, and diazepam have established pediatric dosages. Children must be monitored for both CNS depression and excitability.
- *Older adults:* Older adults may be more susceptible to adverse drug reactions, especially the CNS effects of sedation, dizziness, and possible hallucinations. Reduced doses should be implemented, and safety precautions should be in place. Older adults should be screened for physical conditions, neurological deterioration, or depression, which could be contributing factors to insomnia or anxiety.

Table 13.20 is a drug prototype table for benzodiazepines featuring diazepam. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Benzodiazepine (Schedule IV controlled substance) **Mechanism of Action** Enhances the inhibitory effect of GABA	**Drug Dosage** *Adults:* 2–10 mg orally 2–4 times daily; 5–10 mg intramuscularly or intravenously or 0.2 mg/kg by rectum. *Older or debilitated adults:* 2–5 mg orally 1–2 times/day. *Children ≥6 months:* 0.12–0.8 mg/kg/day orally in divided doses every 6–8 hours.
Indications To relieve anxiety, tension, and nervousness Insomnia As a muscle relaxant Seizures Sleepwalking or night terrors in children Prevention of agitation and delirium tremens in alcohol withdrawal **Therapeutic Effects** Decreases neuronal excitability Enhances action of GABA	**Drug Interactions** CNS depressants Opioids Calcium channel blockers Cimetidine Disulfiram **Food Interactions** Alcohol
Adverse Effects Sedation/drowsiness Ataxia Memory disturbances Confusion Disinhibition Shallow breathing Sleep driving Headaches Depressed mood with/without suicidal ideations Dry mouth Constipation Elevated liver enzymes Urinary retention and hesitancy Blood disorders/anemia	**Contraindications** Hypersensitivity to drug or any of its ingredients Clients <6 months of age Myasthenia gravis Severe respiratory insufficiency Severe hepatic insufficiency Sleep apnea Acute narrow-angle glaucoma Caution: Depression/suicidal ideations

TABLE 13.20 **Drug Prototype Table: Diazepam** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Benzodiazepines

Concomitant use of benzodiazepines with opioids can result in profound sedation, respiratory depression, coma, or death.

Midazolam, when given intravenously, can cause significant respiratory depression that may lead to hypoxia, brain damage, or death.

Nonbenzodiazepine Sedative-Hypnotics

This classification produces sleep. Clients may receive nonbenzodiazepine sedative-hypnotics prior to diagnostic or surgical procedures or take them for sleepless nights. These drugs should only be taken when insomnia is causing distress and nonpharmacologic measures have been ineffective. They should not be taken every night unless absolutely necessary. Intermittent administration can help maintain the drug's effectiveness and also prevent dependence. Additionally, it reduces disturbances of normal sleep patterns.

The loss of awareness to and reaction of environmental stimuli is termed *sedation*. This may be a desirable characteristic for some clients who are restless, nervous, or overreactive to certain stimuli. A sedative is a drug that depresses the central nervous system (CNS). Although a sedative is used more as an anxiolytic, it frequently leads to drowsiness. A hypnotic causes extreme sedation and is used in individuals to promote sleep. These drugs act on the RAS and block the brain's response to incoming stimuli:

- *Eszopiclone (Schedule IV):* Eszopiclone is one of two drugs used long-term (12 months or longer) for chronic insomnia. Studies have shown that clients did not experience tolerance to the hypnotic benefits over a 6-month period (DailyMed, *Eszopiclone*, 2022). Its mechanism of action is due to an interaction with GABA receptors close to or coupled with benzodiazepine receptors. Adverse effects associated with this drug include reduced inhibition, aggression or bizarre behavior, worsening depression and suicidal ideations, hallucinations, and **anterograde amnesia** (memory loss). Many clients report an unpleasant taste of the drug. Clients who take eszopiclone should allow for 8 hours of sleep because it increases total sleep time and reduces sleep latency. It has no effect on reducing nighttime awakenings. Clients should take the drug immediately prior to going to bed due to its rapid onset. The medication should not be taken immediately following a high-fat meal because it can delay the onset by 1 hour.

SAFETY ALERT

Beers Criteria®

Eszopiclone should be avoided in older adults.

(Source: American Geriatrics Society, 2023)

- *Ramelteon (not a controlled substance):* Ramelteon is a melatonin receptor agonist used long-term for chronic insomnia. This drug is beneficial for decreasing sleep latency. ADRs specific to this drug include hormonal effects due to increased levels of prolactin, reduced cortisol levels, and decreased testosterone. Other ADRs include headaches, dizziness, myalgia, arthralgia, abnormal thoughts and/or behaviors, impaired mental alertness, and alteration in taste. This drug should not be taken following a high-fat meal because it will delay the onset of action. Caution must be used in clients with depression and respiratory conditions, such as sleep apnea, because the drug can worsen these. This drug is contraindicated in clients with severe hepatic impairment.
- *Zaleplon (Schedule IV):* Zaleplon is used for short-term treatment (7–10 days) for insomnia. It can help people initiate sleep (decreases sleep latency). The drug does not increase total sleep time or decrease the number of awakenings due to its short half-life. Severe hepatic insufficiency is a contraindication. Clients with mild to moderate hepatic impairment can receive lower doses with frequent follow-up to assess worsening liver failure.
- *Zolpidem (Schedule IV):* Zolpidem is a CNS depressant used for short-term treatment of insomnia associated with difficulties with sleep initiation.
- *Suvorexant (Schedule IV):* Suvorexant belongs to a new class of drugs used to treat insomnia called orexin receptor antagonists. The orexin signaling system is thought to be a central promotor of wakefulness. Blocking these sites suppresses the drive to wake up. For safety purposes, the client should be in bed within 30 minutes of taking the drug. The client should anticipate being in bed for 7 hours.
- *Lemborexant (Schedule IV):* Lemborexant is an orexin receptor antagonist indicated for the treatment of adult clients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance. It can cause the same adverse effects as zolpidem. Sleep onset may be delayed if lemborexant is taken with or soon after a meal.
- *Daridorexant (Schedule IV):* Daridorexant is also an orexin receptor antagonist. It has the same mechanism of action and indications for use as lemborexant. Food also can delay the onset of its effect.

Table 13.21 lists common nonbenzodiazepine sedative-hypnotics and typical routes and dosing for adult clients. Nonbenzodiazepine sedative-hypnotics are either not recommended in children or the safety, efficacy, and dose have not been established.

Drug	Routes and Dosage Ranges
Eszopiclone (Lunesta)	*Adults:* 1 mg orally at bedtime to promote sleep. May increase to 3 mg if needed. *Older adults, debilitated clients, and those with hepatic impairment:* 1 mg orally at bedtime. May increase to 2 mg if needed.
Zaleplon (Sonata)	*Adults:* 10 mg orally at bedtime. Maximum dose: 20 mg orally at bedtime. *Low-weight older adults and those with mild to moderate hepatic impairment:* 5 mg orally at bedtime.
Zolpidem (Ambien)	*Immediate-release tablet:* 5 mg for females and 5–10 mg for males orally at bedtime. *Sublingual tablet:* 1.75 mg for females and 3.5 mg for males orally once per night as needed if the client wakes during the night and has difficulty returning to sleep. *Extended-release tablet:* 6.25 mg for females and 6.25–12.5 mg for males orally at bedtime.
Ramelteon (Rozerem)	8 mg orally at bedtime. Must take within 30 minutes of going to bed.
Suvorexant (Belsomra)	10–20 mg orally within 30 minutes of bedtime with at least 7 hours remaining before planned awakening.
Lemborexant (Dayvigo)	5 mg orally once per night, immediately before going to bed, with at least 7 hours remaining before planned awakening. Maximum dose: 10 mg nightly.
Daridorexant (Quviviq)	25–50 mg once per night, taken orally within 30 minutes before going to bed, with at least 7 hours remaining prior to planned awakening.

TABLE 13.21 **Drug Emphasis Table: Nonbenzodiazepine Sedative-Hypnotics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Clients can experience **angioedema** if they are allergic to any of the components in the drug. These drugs are metabolized by the liver, so they should be avoided by anyone with severe hepatic failure. Lower doses should be administered for those with mild to moderate hepatic insufficiency and in the older adult. Glaucoma, psychosis, and acute alcohol intoxication can be exacerbated by the CNS depression of these drugs. Due to the potential for respiratory depression, clients with a history of COPD or sleep apnea should use caution. If taking a nonbenzodiazepine sedative-hypnotic for at least 1 week, gradual tapering is crucial when discontinuing. If stopped abruptly, withdrawal syndrome can occur including nausea, headache, vertigo, nightmares, and seizures. Rebound insomnia can potentially occur but only lasts a few days after the drug has been stopped. Essentially, it resolves on its own.

Lemborexant and daridorexant are both contraindicated for the use in narcolepsy. It has been advised that these two drugs should not be used in the presence of hepatic disease. The safety and effectiveness in those under age 18 has not been established.

Concurrently taking another CNS depressant or drinking alcohol with this medication can intensify CNS depression and cause excessive drowsiness along with respiratory depression. Both of these can increase the risk for injury.

If a client takes the medication directly after consuming a high-fat meal, it can significantly delay absorption of the drug. Herbal supplements should be avoided.

! SAFETY ALERT

Similarly Named Drugs Associated with Nonbenzodiazepine Sedative-Hypnotics

Do not confuse:

- Lunesta (nonbenzodiazepine sedative-hypnotic) with Neulasta (bone marrow stimulant)
- Rozerem (nonbenzodiazepine sedative-hypnotic) with Razadyne (acetylcholinesterase inhibitor for dementia)

(Source: ISMP, 2023)

Table 13.22 is a drug prototype table for nonbenzodiazepine sedative-hypnotics featuring zolpidem. It lists drug

class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nonbenzodiazepine sedative-hypnotics (Schedule IV controlled substance) **Mechanism of Action** Selectively binds to specific GABA receptors	**Drug Dosage** *Immediate-release tablet:* 5 mg for females and 5–10 mg for males orally at bedtime. *Sublingual tablet:* 1.75 mg for females and 3.5 mg for males orally once per night as needed if the client wakes during the night and has difficulty returning to sleep. *Extended-release tablet:* 6.25 mg for females and 6.25–12.5 mg for males orally at bedtime.
Indications Immediate-release form: Short-term treatment (7–10 days) for insomnia Extended-release form: Decreases sleep latency and increases total sleep time **Therapeutic Effects** Reduces sleep latency and increases sleep time	**Drug Interactions** CNS depressants (antihistamines, kava, valerian) Opioids **Food Interactions** Alcohol High-fat meals
Adverse Effects Daytime drowsiness Reduced inhibition Aggression Worsening depression and suicidal ideations Hallucinations Abnormal dreams Anterograde amnesia Headache/dizziness Sleep driving Unpleasant taste Withdrawal syndrome—rebound insomnia Respiratory depression Tolerance can occur after 2 weeks	**Contraindications** Hypersensitivity Severe hepatic impairment Caution: COPD Sleep apnea Pregnancy and lactation Depression Impaired hepatic function Impaired respiratory function

TABLE 13.22 **Drug Prototype Table: Zolpidem** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Beers Criteria®

Sedative-hypnotics should be avoided in older adults (age 65 or older) because of associated risks including memory problems, drowsiness, increased risk of falls, and increased risk of having a motor vehicle collision.

(Source: Lee & Green, 2019)

Nursing Implications

The nurse should do the following for clients who are taking anxiolytics or sedative-hypnotics:

- Help the client to identify triggers and develop coping mechanisms to help with reducing anxiety.
- Assess the client's sleep patterns.
- Monitor heart rate, blood pressure, respiratory rate, temperature, and weight.
- Assess level of consciousness and orientation.
- Evaluate mood for anger, aggression, or hallucinations (paradoxical response).
- Assess for signs/symptoms of dependence, overdose, and withdrawal, such as psychomotor agitation,

insomnia, headache, tremor, palpitations, psychosis, and seizures.
- Monitor renal and liver function tests and CBC.
- Modify the environment to promote sleep (dim lights, turn off television).
- Relieve symptoms that are interfering with sleep, such as analgesics for pain or antitussives for cough.
- Provide safety precautions when the client is ambulatory.
- Instruct the client that the immediate-release formulation is used to help them fall asleep and that the extended-release formulation is used to maintain sleep throughout the night.
- Use a large muscle when administering the intramuscular (IM) preparation. Inject it slowly and rotate sites.
- Monitor injection sites for local reactions and institute care immediately.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking drugs for anxiety and sleep disorders should:

- Understand the drug will reduce the symptoms but does not cure the underlying problem.
- Verbalize the importance of attending counseling to learn ways to manage their anxiety.
- Identify nondrug measures to manage stress and promote sleep, such as relaxation techniques and hobbies.
- Limit the daily consumption of caffeine and avoid caffeine close to bedtime.
- Establish a bedtime routine to consistently follow.
- Increase physical activity.
- Take the sedative-hypnotic just before going to bed so the client is lying down when the drug begins to work.
- Notify the provider if experiencing any hallucinations or thoughts of suicide.
- Avoid daytime naps.
- Place sublingual tablets under the tongue and allow them to dissolve.
- Only use as needed and for the shortest duration.

The client taking drugs for anxiety and sleep disorders *should not:*

- Stop any drug abruptly due to withdrawal syndrome and the risk of seizures in epileptic clients.
- Chew, crush, or break in half any extended-release tablets/capsules.
- Use these on a long-term basis.
- Take any stimulant drugs, such as cold remedies or appetite suppressants.
- Engage in activities that require alertness until the effects of the drug are known.
- Take nonbenzodiazepines with a high-fat meal due to delayed absorption.
- Consume any caffeinated beverages/foods or excess water during evening hours.
- Swallow the sublingual tablets or take with water.
- Consume any alcohol.

13.5 CNS Stimulants and Nonstimulants

LEARNING OUTCOMES

By the end of this section, you should be able to:
- 13.5.1 Identify the characteristics of drugs used to treat attention deficit disorders and narcolepsy.
- 13.5.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of drugs used to treat attention deficit disorders and narcolepsy.
- 13.5.3 Describe nursing implications for drugs used in the treatment of attention deficit disorders and narcolepsy.
- 13.5.4 Explain the client education related to drugs used in the treatment of attention deficit disorders and narcolepsy.

Attention deficit hyperactivity disorder (ADHD) is the most common psychiatric or neurobehavioral disorder in

children. ADHD is more prevalent among males than females (NIMH, 2022). Various theories have been proposed regarding the actual etiology; however, no single theory has been accepted. This condition is characterized by persistent behavior demonstrating inattention, impulsivity, and/or hyperactivity that generally presents during childhood but can persist into adulthood (American Psychiatric Association, 2022). ADHD can be divided into three subcategories: predominantly inattentive type, predominantly hyperactive-impulsive type, or combined type (NIMH, 2022).

The goal of drug therapy is to control symptoms, facilitate learning, and promote social development. Commonly used agents are CNS stimulants, which are considered the first-line treatments for ADHD. These work by increasing the brain chemicals dopamine and norepinephrine, which play essential roles in thinking and attention. If a client is unable to tolerate the stimulant agents, nonstimulating drugs can be tried. Treatment includes a combination of medications, **cognitive behavioral therapy**, support groups and other therapies, stress management, and academic accommodations (NIMH, 2022).

Narcolepsy is a chronic neurological disorder characterized by excessive daytime sleepiness and sudden periods of sleep attacks at inopportune times. The cause is not completely understood but is possibly caused by several factors including autoimmune disorders, family history, or brain trauma (National Institute of Neurological Disorders and Stroke, n.d.). This condition affects males and females equally and usually begins during the teenage or young adult years. Most clients verbalize that the excess sleepiness substantially interferes with their daily lives, including work, school, home, and social life. **Cataplexy** is another common feature of narcolepsy. This condition is exhibited by loss of muscle function, ranging from slight weakness to complete body collapse. These episodes are frequently triggered by strong emotional reactions, such as laughing, anger, surprise, or fear, and last a duration of a few seconds to minutes. Cataplexy can occur several times per day to a few times a year. Other clinical manifestations of narcolepsy include **hypnagogic hallucinations** (sleep-related hallucinations that occur when falling asleep) and **sleep paralysis** (temporary inability to move when falling asleep or waking). Medications and lifestyle changes can manage the symptoms of narcolepsy (National Institute of Neurological Disorders and Stroke, n.d.).

Central Nervous System Stimulants

CNS stimulants are the mainstay of ADHD therapy. Although treating ADHD with a stimulant seems paradoxical, these drugs give the client the ability to maintain attention and focus on one activity for a longer period of time. These drugs redirect and excite the arousal stimuli from the RAS. They also help clients increase goal-oriented behavior. The impulsiveness and hyperactivity decline because clients are now able to concentrate on the task at hand. These drugs work by increasing the release of catecholamines from presynaptic neurons. In addition, amphetamines block the reuptake of NE and dopamine, which further increases their concentration so more of the drug can bind to the postsynaptic neuron. It is valuable to know that if one stimulant is ineffective, another should be tried before considering a nonstimulant.

The dosing schedule is important and is determined by the time course of the formulation selected. Most of these are available in immediate-release (IR), sustained release (SR), and 24-hour formulations. Most are controlled substances, and education should be provided to ensure these are not inappropriately used or distributed.

The most common CNS stimulants are:

- *Methylphenidate (Class II controlled substance):* This medication is a first-line treatment for ADHD and a second-line treatment for narcolepsy.
- *Amphetamine/dextroamphetamine (Class II controlled substance):* This is a mixed-salt drug available in IR and ER formulations. The mechanism of action is to mediate CNS stimulation through the release of norepinephrine and dopamine. This is the only FDA-approved stimulant for use in children under age 3.
- *Dextroamphetamine:* This drug releases NE from nerve terminals and increases the amounts of NE, dopamine, and serotonin.
- *Lisdexamfetamine:* This is a **prodrug** of dextroamphetamine. It is used only in the treatment of ADHD and, recently, binge-eating disorders among adults. It is not approved for use in narcolepsy or as a weight-loss measure.
- *Methamphetamine:* This is a highly addictive drug used to treat ADHD and narcolepsy. It is frequently used recreationally, and it is at high risk of being obtained and distributed for nontherapeutic uses.
- *Dexmethylphenidate:* This drug is used to treat ADHD in clients age 6 and older. As with all stimulants,

pediatric clients taking this medication should be monitored for evidence of hindered growth and development.

- *Modafinil (Class IV controlled substance):* This drug improves wakefulness in clients with excessive daytime sleepiness associated with narcolepsy or shift-work sleep disorder and is used as an adjunctive therapy for obstructive sleep apnea/hypopnea syndrome. The drug can also be used to treat ADHD. Clients need to be aware that this drug can decrease the effectiveness of oral contraceptives.
- *Pitolisant:* This is an H3 (histamine) blocker, not a controlled substance. It is used to treat excessive daytime sleepiness caused by narcolepsy and to treat cataplexy in adults with narcolepsy.

Table 13.23 lists common CNS stimulants and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Methylphenidate (Concerta, Ritalin, Daytrana)	*ADHD:* *Adults: Immediate release:* Initial dose: 10–60 mg daily in 2–3 divided doses. *Extended release:* Initial dose: 20 mg in the morning; maximum dose: 60 mg/day. *Transdermal:* Apply 10 mg patch to hip 2 hours before effect is needed. Remove 9 hours after application. *Children ≥6 years: Immediate release:* 5 mg twice daily. *Narcolepsy:* *Immediate release:* Initial dose: 10 mg 2–3 times/day. Maximum dose: 60 mg/day.
Amphetamine and dextroamphetamine (Adderall)	*ADHD:* *Adults: Immediate release:* Initial dose: 5 mg 1–2 times/day. Maximum dose: 40 mg/day. *Extended release:* Initial dose: 20 mg in the morning. Maximum dose: 60 mg/day. *Children 3–5 years: Immediate-release:* 2.5 mg/day; maximum dose: 30 mg/day. *Children ≥6 years: Immediate-release*: 5 mg 1–2 times per day. *Extended-release:* 5–10 mg/day; maximum dose: 30 mg/day. *Narcolepsy:* *Adults and children >12 years: Immediate release:* Initial dose: 10 mg/day; maximum dose: 60 mg/day. *Children 6–12 years:* Initial dose: 5 mg/day.
Dextroamphetamine (Xelstrym)	*ADHD:* *Adults:* Initial dose: 9 mg/9 hours transdermally. Maximum dose: 18 mg/9 hours. Apply transdermally 2 hours before an effect is needed and remove within 9 hours. *Children (6–17 years):* Initial dose: 4.5 mg/9 hours transdermally. Titrate dosage in weekly increments of 4.5 mg up to a maximum recommended dose of 18 mg/9 hours.
Lisdexamfetamine (Vyvanse)	*ADHD:* *Adults and children ≥6 years:* Initial dose: 30 mg/day in the morning; may increase by 10–20 mg at weekly intervals until optimal response is reached. Maximum dose: 70 mg/day.
Methamphetamine (Desoxyn)	*ADHD:* *Adults and children ≥6 years:* Initial dose: 5 mg 1–2 times daily. Usual effective dose: 20–25 mg/day in 2 divided doses.
Dexmethylphenidate (Focalin)	*ADHD:* *Adults and children ≥6 years:* Initial dose: 2.5 mg orally twice daily, 4 hours apart; maximum dose: 10 mg twice daily.

TABLE 13.23 **Drug Emphasis Table: CNS Stimulants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Serdexmethylphenidate and dexmethylphenidate (Azstarys)	*ADHD:* *Adults and children 13–17 years:* Initial dose: 39.2 mg/7.8 mg/day in the morning; dosage may be increased after 1 week to 52.3 mg/10.4 mg/day. *Children 6–12 years:* Initial dose: 39.2 mg/7.8 mg orally once daily in the morning; dosage may be increased to 52.3 mg/10.4 mg daily or decreased to 26.1 mg/5.2 mg daily after 1 week. Maximum dose: 52.3 mg/10.4 mg/day.
Modafinil (Provigil)	*ADHD:* Initial dose: 100–300 mg/day. *Narcolepsy and obstructive sleep apnea/hypopnea syndrome:* Initial dose: 200 mg/day taken in the morning. *Shift-work sleep disorder:* Initial dose: 200 mg/day taken 1 hour prior to shift work. Dose must be reduced by 50% in clients with severe hepatic impairment.
Pitolisant (Wakix)	*Narcolepsy:* *Adults and children ≥13 years:* Administer once daily in the morning. Recommended dose: 17.8–35.6 mg/day orally. Week 1: Initiate with 8.9 mg/day orally. Week 2: Increase dose to 17.8 mg/day orally. Week 3: May increase to the maximum recommended dosage of 35.6 mg/day orally.

TABLE 13.23 **Drug Emphasis Table: CNS Stimulants** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Similarly Named Drugs Associated with CNS Stimulants

Do not confuse Adderall (CNS stimulant) with Inderal (beta blocker).

(Source: ISMP, 2023)

Adverse Effects and Contraindications

A client must use CNS stimulants with caution when pregnant and taking stimulants. Premature delivery and low birth weight have occurred in infants born to a parent taking these drugs.

Stimulants are contraindicated in glaucoma, hyperthyroidism, and the spectrum of cardiovascular diseases because they can exacerbate these conditions. Individuals with a history of drug or alcohol use disorder/dependence should avoid these drugs because they have a high potential for physical and psychological dependence. Sudden cardiac arrest has occurred with the use of CNS stimulants. Studies have shown that the majority of these cases occurred in children with an undocumented cardiac defect. It is now recommended to obtain a baseline electrocardiogram (ECG, EKG) before beginning this therapy. To reduce the risk of insomnia, these medications should be taken in the morning or early afternoon. If a client has been diagnosed with a psychiatric disorder, they should avoid the CNS stimulants because they can worsen the preexisting psychiatric disorder. Motor and verbal tics can be intensified with the CNS stimulants, so it is essential to identify if there is a family history or personal diagnosis of Tourette syndrome.

The effects of phenytoin and tricyclic antidepressants (TCAs) are increased by the CNS stimulants. Also, lisdexamfetamine should not be used concurrently with TCAs or meperidine because it can potentiate the effects of these drugs, increasing the risk of adverse effects. MAOIs are contraindicated if currently taking or within 14 days of receiving the last dose because both CNS stimulants and MAOIs can drastically increase blood pressure. The effects of alpha-1 adrenergic blockers can be reduced or negated by the CNS stimulants.

Table 13.24 is a drug prototype table for CNS stimulants featuring methylphenidate. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class CNS stimulant (Class II controlled substance) **Mechanism of Action** Blocks the reuptake of norepinephrine and dopamine in specific areas of the brain	**Drug Dosage** *ADHD:* *Adults: Immediate release:* Initial dose: 10–60 mg daily in 2–3 divided doses. *Extended release:* Initial dose: 20 mg in the morning; maximum dose: 60 mg/day. *Transdermal:* Apply 10 mg patch to hip 2 hours before effect is needed. Remove 9 hours after application. *Children ≥6 years: Immediate release:* 5 mg twice daily. *Narcolepsy:* *Immediate release:* Initial dose: 10 mg 2–3 times/day. Maximum dose: 60 mg/day.
Indications ADHD Narcolepsy Traumatic brain injury (TBI) **Therapeutic Effects** Enhances dopamine and NE actions in certain brain regions to improve attention, concentration, and wakefulness Enhancement of dopamine in the basal ganglia may improve hyperactivity	**Drug Interactions** Concomitant use of MAOIs or within 14 days of MAOI use Alpha-1 adrenergic blockers Phenytoin Tricyclic antidepressants Meperidine **Food Interactions** Alcohol Caffeine
Adverse Effects Insomnia Headaches/seizures Heart palpitations/tachyarrhythmias Angina Sudden cardiac death CVA Hypertension Leukopenia and anemia Hyperhidrosis Irritability/nervousness Anorexia/weight loss Potential for dependence and misuse Suppression of growth in children with long-term use Exacerbation of preexisting or emergence of new psychiatric disorders such as psychosis or mania Contact dermatitis with transdermal application	**Contraindications** Advanced arteriosclerosis Symptomatic cardiovascular disease Congenital cardiac structural abnormalities Recent MI or angina Severe hypertension Heart failure Arrhythmias Hyperthyroidism Glaucoma History of substance use History of psychiatric disorders Family history or personal diagnosis of Tourette syndrome Caution: Pregnancy/breastfeeding Seizures

TABLE 13.24 **Drug Prototype Table: Methylphenidate** (source: https://dailymed.nlm.nih.gov/dailymed/)

CNS Nonstimulants

These alternative drugs for ADHD and narcolepsy are not associated with the many cardiac and systemic stimulatory effects experienced with the CNS stimulants. They are preferable in clients who are unable to tolerate the stimulatory effects of the other drugs. The most common CNS nonstimulants are:

- *Atomoxetine:* This is an SNRI with anticholinergic effects used to treat ADHD. It inhibits reuptake of NE in nerve synapses. It has little risk for abuse and dependence; therefore, it is not a controlled substance.
- *Guanfacine:* This is a selective alpha-2 adrenergic agonist. It is not a controlled substance. Guanfacine does not produce CNS stimulation but instead can cause significant CNS depression. As an alpha-2 agonist,

sympathetic nerve impulses are reduced. Furthermore, it binds specifically to postsynaptic alpha-2A adrenoreceptors in the prefrontal cortex. As a result, working memory and behavioral inhibitions are affected, which improves symptoms associated with ADHD.

- *Clonidine:* This is an alpha-2 adrenergic agonist. The mechanism of action in ADHD is unknown.
- *Viloxazine:* This drug is a selective NE reuptake inhibitor for the treatment of ADHD in adults and pediatric clients age 6 and older.
- *Solriamfetol:* This drug is a dopamine and norepinephrine reuptake inhibitor (DNRI) that improves daytime wakefulness in adult clients with narcolepsy or obstructive sleep apnea (OSA).
- *Sodium oxybate (Class III controlled substance):* This is the first once-at-bedtime medication for people with narcolepsy. The extended-release formulation treats cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy. It has not been tested in children or pregnant individuals; therefore, it must be avoided in these populations. This CNS depressant drug is the sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB is associated with CNS adverse reactions, including seizure, respiratory depression, decreased consciousness, coma, and death. It is available only through a restricted program called the Lumryz REMS. It is contraindicated in combination with sedative-hypnotics or alcohol. Adverse effects include depression and suicidality, confusion/anxiety, and **parasomnias**. Ingesting high sodium content while taking this drug can exacerbate heart failure or hypertension or further impair renal function.

Table 13.25 lists common CNS nonstimulants and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Atomoxetine (Strattera)	*Adults and children >70 kg:* 40 mg/day orally. Gradually increase to a target daily dose of 80 mg. Maximum dose: 100 mg/day. *Children ≤70 kg:* Initial dose: 0.5 mg/kg/day; target dose: 1.2 mg/kg/day; maximum dose: 1.4 mg/kg/day.
Guanfacine (Intuniv)	*Adults and children ≥6 years: Extended-release tablet:* Initial dose: 1 mg/day; maximum dose: 4–7 mg/day.
Clonidine (Kapvay)	*Adults and children >6 years:* Initial dose: 0.1 mg/day tablet at bedtime for 1 week. Increase daily dosage in increments of 0.1 mg/day each week until desired response is achieved.
Viloxazine (Qelbree)	*Adults:* Initial dose: 200 mg/day orally; increase dose as needed and tolerated; maximum dose: 600 mg/day. *Children 12–17 years:* Initial dose: 200 mg/day orally; increase dose as needed and tolerated; maximum dose: 400 mg/day. *Children 6–11 years:* Initial dose: 100 mg/day orally; increase dose as needed and tolerated; maximum dose: 400 mg/day. *Children <6 years:* Use and dose must be determined by the provider.
Solriamfetol (Sunosi)	*Narcolepsy:* Initial dose: 75 mg/day orally; maximum dose: 150 mg/day orally. *Sleep apnea:* Initial dose: 37.5 mg/day orally; maximum dose: 150 mg/day orally. *Adults:* Administer once daily upon awakening. Avoid administration within 9 hours of planned bedtime due to potential to interfere with sleep. *Children:* Safety and effectiveness have not yet been established.
Sodium oxylate (Lumryz)	*Narcolepsy:* Initial dose: 4.5 g orally once nightly; titrate in increments of 1.5 g per night at weekly intervals. Recommended dose: 6–9 g once per night orally.

TABLE 13.25 Drug Emphasis Table: CNS Nonstimulants (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects seen with atomoxetine are mainly related to its anticholinergic effects. These include dry mouth, blurred vision, nausea, constipation, and urine retention. Guanfacine and clonidine can cause sedation, severe hypotension, and bradycardia. Antihypertensives and CNS depressants are contraindicated with these due to the additive effects they can have on blood pressure and sedation. Taking guanfacine with a high-fat meal can cause

increased absorption of the drug.

TCAs can increase blood pressure and may counteract clonidine's hypotensive effects. Monitor blood pressure and adjust as needed. Antihypertensive agents will potentiate the hypotensive effects of clonidine. CNS depressants can potentiate sedating effects. It is recommended to avoid concomitant use. Digoxin, calcium channel blockers, and beta blockers should not be used in conjunction with clonidine because they can exacerbate bradycardia and AV block.

SAFETY ALERT

Similarly Named Drugs Associated with CNS Nonstimulants

Do not confuse Intuniv (CNS nonstimulant) with Invega (antipsychotic).

(Source: ISMP, 2023)

Table 13.26 is a drug prototype table for CNS nonstimulants featuring clonidine. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class CNS nonstimulant, alpha-2 adrenergic agonist **Mechanism of Action** Unknown	**Drug Dosage** *Adults and children >6 years:* Initial dose: 0.1 mg/day tablet at bedtime for 1 week. Increase daily dosage in increments of 0.1 mg/day each week until desired response is achieved.
Indications ADHD as a monotherapy or as an adjunct to a CNS stimulant **Therapeutic Effects** Reduces sympathetic outflow from the CNS	**Drug Interactions** Tricyclic antidepressants Antihypertensive agents CNS depressants Drugs that affect sinus node function or AV node conduction (digoxin, calcium channel blockers, and beta blockers) **Food Interactions** No significant interactions
Adverse Effects Hypotension Bradycardia/syncope Sedation Rebound hypertension with abrupt withdrawal Allergic reactions (generalized rash, angioedema)	**Contraindications** Hypersensitivity to any of the ingredients Caution: Heart block Cardiovascular disease Cerebrovascular disease Chronic renal failure

TABLE 13.26 Drug Prototype Table: Clonidine (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking CNS stimulants and nonstimulants:

- Screen and monitor client's cardiovascular risk factors, such as family history, smoking, elevated lipids, hypertension, diabetes mellitus, and obesity.
- Assess client's psychiatric history.
- Measure and document blood pressure readings, heart rate, weight, food intake, and amount of uninterrupted sleep.
- Obtain a baseline ECG prior to beginning therapy and during episodes of chest pain or palpitations.
- Provide drug holidays to children for the purpose of determining the need for continued treatment and allow

for “catch-up” growth.
- Monitor for improved attention span and task performance in both children and adults.
- Observe for a decrease in hyperactivity in children along with functioning appropriately during social interactions with other children.
- Assess for fewer sleep episodes during normal waking hours.
- Ensure nutritional needs are being met.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a CNS stimulant or nonstimulant should:

- Report chest pain, difficulty breathing, fainting, abnormal thinking or behavior, increased aggression, hallucinations, and unintended weight loss.
- Take immediate-release tablets, chewable tablets, and solution 30–45 minutes before meals.
- Drink at least 8 oz of water with chewable tablets to avoid choking.
- Weigh self at least once a week.
- Be cognizant of caloric and nutrient intake to avoid excessive weight loss.

The client taking a CNS stimulant or nonstimulant *should not:*

- Chew or crush sustained- or extended-release formulations.
- Take a CNS stimulant after 6 p.m or less than 6 hours before bedtime.
- Take less than 1 tablet per day.
- Take guanfacine with a high-fat meal.
- Take more than prescribed or distribute to others.
- Drive or participate in any activities that require alertness until the effects of nonstimulants are known.

FDA BLACK BOX WARNING

CNS Stimulants and Nonstimulants

Atomoxetine, viloxazine: In clinical studies, higher rates of suicidal thoughts and behavior were reported in clients with ADHD treated with atomoxetine or viloxazine than in clients treated with placebo.

Dextroamphetamine, lisdexamfetamine, and **dexmethylphenidate** have a high misuse potential.

Sodium oxybate has a risk of causing clinically significant respiratory depression. This medication also has a high risk of abuse or misuse.

Chapter Summary

This chapter discussed various common mental health disorders and the drug classifications used in managing them. Some of these classifications can be used in more than one disorder. Likewise, multiple drug classifications can be used in treating a single mental health condition. Several of these classifications are associated with maintaining a balance of the neurotransmitters involved. For instance, antidepressants such as SSRIs, SNRIs, and NDRIs increase neurotransmitters' availability to receptors for longer periods of time. Mood stabilizers, such as lithium, are beneficial in preventing or reducing fluctuations in mood. Antipsychotics are useful in treating the symptoms of schizophrenia. Overall, these drugs can enhance the ability of clients to have the opportunity to live an independent life and be a positive contributor to society. As further research expands our knowledge base, it will continue to alter the treatment of mental health disorders. Furthermore, as the new growth of information is shared, it can play a major role in diminishing the stigma long associated with mental-health illness.

Key Terms

affective relates to mood, feelings, emotion, and attitudes

akathisia continuous restlessness, inability to sit still; clients may say they feel hyperactive deep inside their body

angioedema fluid buildup in the deeper layers of the skin causing edema; considered a type of allergic reaction

anterograde amnesia short-term memory loss

anxiety a feeling of nervousness, apprehension, and/or worry about a future threat

anxiolytics drugs that treat anxiety

asociality lack of interest in social interactions

avolition total lack of motivation

bipolar disorder a disorder that causes intense changes in a person's mood (ranging from manic to depressive), energy, and ability to function

cardiotoxicity adverse drug reactions that can negatively affect the structure and function of the heart

cataplexy associated with narcolepsy; brief loss of voluntary muscle tone triggered by strong emotion

catatonia state in which someone is awake but does not appropriately respond to other people and their environment; can affect someone's movement, speech, and behavior

cognitive-behavioral therapy type of psychotherapeutic method that helps people identify maladaptive and negative patterns of thinking that cause a negative influence on behavior and mood; this thinking is challenged and replaced with more desirable, realistic thoughts.

cytochrome P450 enzyme system enzymes responsible for breaking down drugs to their active or inactive metabolites; these can be inhibited or induced by drugs altering drug metabolism

depot injection an injection that releases medication very slowly so it increases the duration of action

depression a disorder in which the person experiences feelings of sadness, anger, frustration, hopelessness, and helplessness

dystonia spasms of the tongue, neck, back, and legs; the spasms may cause unnatural positioning of the neck and eyes and excessive salivation

extrapyramidal symptoms (EPS) variety of movement disorders, such as tardive dyskinesia, akathisia, or bradykinesia, experienced as a result of taking dopamine antagonists

hyperpyrexia drug-induced elevation of body temperature and muscle rigidity

hypersomnia excessive sleeping at night or excessive fatigue during the day

hypnagogic hallucinations sleep-related hallucinations that occur as a person is falling asleep; commonly visual and consist of vivid images of patterns, shapes, or people; occasionally may involve sounds or physical sensations

monoamine a drug molecule that contains a single amine group, such as a neurotransmitter or hormone

paradoxical medication effects when a medication causes an effect opposite to its intended outcome

parasomnia any kind of sleep-related disorder that occurs while going to sleep, during the sleep cycle, or when waking up from sleep; symptoms vary but the most common include nightmares, night terrors, sleep paralysis, grinding teeth, sleepwalking, sleep eating, and sleep talking

prodrug a drug that is pharmacologically inactive until it is ingested and metabolized into an active form

pseudoparkinsonism an adverse effect of antipsychotics that mimics the manifestations of Parkinson's disease, such as shuffling gait, stooped posture, and muscle tremors

psychopharmacology studies the effects that medications can have on the mind

psychosis loss of external reality

psychotropic medication drug that changes the functions of the nervous system and alters a person's mental status
sedative-hypnotic class of drugs used to induce or maintain sleep
sleep latency the amount of time it takes a person to fall asleep once they go to bed
sleep paralysis a temporary inability to move or speak while falling asleep or upon waking
tardive dyskinesia abnormal muscle movements such as lip smacking, tongue darting in and out of mouth, chewing movements without food in mouth, and slow, aimless extremity movements
xerostomia dry mouth; usually due to inadequate fluid intake or can be drug-induced

Review Questions

1. The nurse is teaching a client receiving a tricyclic antidepressant. Which of the following symptoms related to its anticholinergic effects could the client experience?
   a. Increased appetite, diarrhea, and glaucoma
   b. Xerostomia, constipation, and urinary retention
   c. Excessive salivation, tachycardia, and urinary incontinence
   d. Nightmares, increased libido, and blurred vision

2. A client with bipolar disorder has a subtherapeutic lithium level. What will the nurse expect to assess in this client?
   a. A decrease in impulsivity and hyperactivity
   b. Rapid, pressured speech along with interrupting others
   c. Sleeping 6–8 consecutive hours per night
   d. Ability to sit down and eat a well-balanced meal

3. Which of the following observations indicates that lisdexamfetamine has been effective for a 10-year-old diagnosed with ADHD?
   a. The child received two notes from their school due to inappropriate behavior.
   b. The child sleeps 8 hours per night and still falls asleep during the day.
   c. The child is able to sit and play a game for 30 minutes with a friend.
   d. The child has difficulty following verbal instructions from the teacher.

4. A client has been taking fluoxetine for 2 weeks. They tell the nurse they do not think the medication is working because they still feel depressed. What is the nurse's best response?
   a. "This may not be the best medication for you. Let me call the provider to get something different."
   b. "You might still be depressed, but you look and sound a lot better."
   c. "This drug takes about 4–6 weeks before you may see full therapeutic effects."
   d. "I will call the provider and ask if the dosage can be increased."

5. Which adverse effect should the nurse assess for in a client who is taking haloperidol?
   a. Nausea and vomiting
   b. Tremors
   c. Weight loss
   d. Hypertension

6. The nurse has completed medication education for a client prior to their receiving phenelzine. The nurse evaluates the education as effective when the client makes which statement?
   a. "Eating seafood could cause my blood pressure to become very low."
   b. "Instead of white bread, I should use whole wheat."
   c. "I guess I cannot have steak and eggs anymore."
   d. "I should use almond milk instead of whole milk and need to avoid aged cheeses."

7. A hospitalized client was discharged on clozapine. The client is concerned about the potential significant adverse effects. Instructions on the REMS program were explained. To avoid difficulty with obtaining access

immediately after discharge, what would the nurse expect from the inpatient pharmacy to ensure consistency?

a. A 3-day supply will be provided to the client to allow time for them to fill their prescription from their pharmacy.
b. A maximum of a 7-day supply of this medication will be provided upon client discharge.
c. Inpatient pharmacies will dispense a day's supply of clozapine that aligns with the client's monitoring frequency.
d. The inpatient pharmacist will call the client's outside pharmacy to ensure they fill the prescription immediately.

8. Which antidepressant would be the best choice for a client experiencing sexual dysfunction from a selective serotonin reuptake inhibitor (SSRI)?

a. Fluoxetine
b. Venlafaxine
c. Bupropion
d. Phenelzine

9. Zolpidem is the most appropriate choice for clients with which condition?

a. Increased sleep latency and maintaining sleep
b. Difficulty initiating sleep and early morning awakenings
c. Obstructive sleep apnea (OSA) and respiratory problems
d. Maintaining sleep during the night due to anxiety and depression

10. A 10-year-old child is receiving methylphenidate. The parent tells the nurse the child will not sleep while on the medication. What is the best response?

a. "Do not give the medication after 6 p.m."
b. "You can give 25 mg diphenhydramine at bedtime."
c. "Cut the bedtime dose in half so that it will not interfere with sleep."
d. "This is a serious adverse reaction. We will need to contact the provider."

CHAPTER 14
Pain Response Drugs

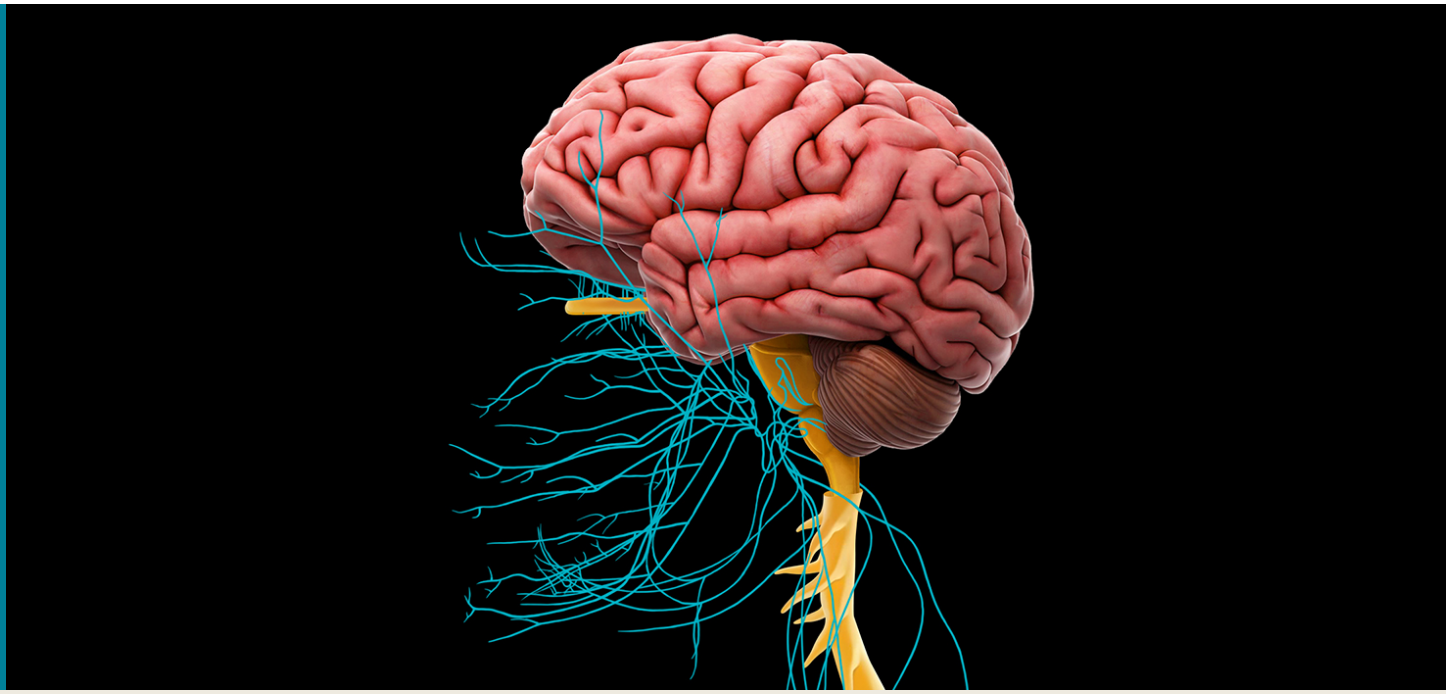


FIGURE 14.1 The nervous system, the body's control center, consists of the brain, the spinal cord, and a very complex system of nerves. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Pain is one of the most common reasons individuals seek medical treatment, and it can arise from a number of sources, including trauma, cancer, and autoimmune and other diseases. When pain and its underlying causes are not managed well, chronic problems such as disability, lost wages, and mental health issues can result. In addition to nonpharmacologic options, pain is often managed with nonopioid analgesics, which include several medications that clients can acquire without a prescription, and opioid agonists, which are reserved for more severe forms of pain and require a prescription. This chapter will review the definition of pain, explain how pain occurs in the body, and describe some ways to treat pain with pharmacologic therapies.

14.1 Introduction to Pain

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 14.1.1 Define pain.
- 14.1.2 Differentiate between acute pain and chronic pain.
- 14.1.3 Explain the pain threshold.

Pain

Pain is generally defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" (Raja et al., 2020). Pain is, by nature, a subjective experience that the client describes to the health care provider, so many health care professionals practically define pain as

"whatever the client says it is." This makes assessing and treating pain a challenge for many health care professionals. This is especially true considering that many health care providers do not receive sufficient training in pain management to always address a client's needs adequately.

Acute pain is typically sudden in onset and will usually have a duration of less than a month. Acute pain is commonly caused by events such as trauma, injury, or certain medical treatments such as surgery. **Chronic pain** typically lasts longer than 3 months. Common causes of chronic pain include inflammation and medical treatments, or the cause can be entirely unknown (idiopathic pain). Because of the chronic nature of this type of pain, affected individuals are more likely to develop long-term complications such as depression, anxiety, substance use disorders, and chronic disability. The Institute of Medicine Committee on Advancing Pain Research, Care, and Education estimates that more than 100 million people in the United States live with some form of chronic pain and that chronic pain costs more than $600 billion each year in terms of medical treatment and lost productivity (Smith & Hillner, 2019).

In addition to acute and chronic classifications of pain, pain can be characterized in ways that can help determine the most appropriate plan for managing it. **Nociceptive pain** is pain that arises from injury to bodily tissue, such as pain related to traumatic injury, surgery, or infection. This type of pain may be described as a sharp, dull, or stabbing sensation. Nociceptive pain can be further classified as either somatic or visceral pain. Somatic pain typically occurs in parts of the body such as the skin, bones, and muscles. It tends to be easily pinpointed, may be described as sharp, and is localized to the injured tissue. Visceral pain affects internal organs such as the stomach and liver. It may be described as deep, dull, aching sensations that can be more difficult to localize. In some cases, deep visceral pain may cause pain elsewhere in the body, which is known as **referred pain** (e.g., pancreatic injury causing back pain, myocardial infarction causing jaw and shoulder pain; see Figure 14.2).

In contrast to nociceptive pain, **neuropathic pain** is pain that arises from the nerves of the peripheral and central nervous systems. Neuropathic pain can result from various neurologic conditions, such as diabetic neuropathies, stroke, multiple sclerosis, herpes zoster (shingles), and phantom limb pain related to an amputation. Neuropathic pain is often described as burning, tingling, or shooting pains that radiate from one location to another.

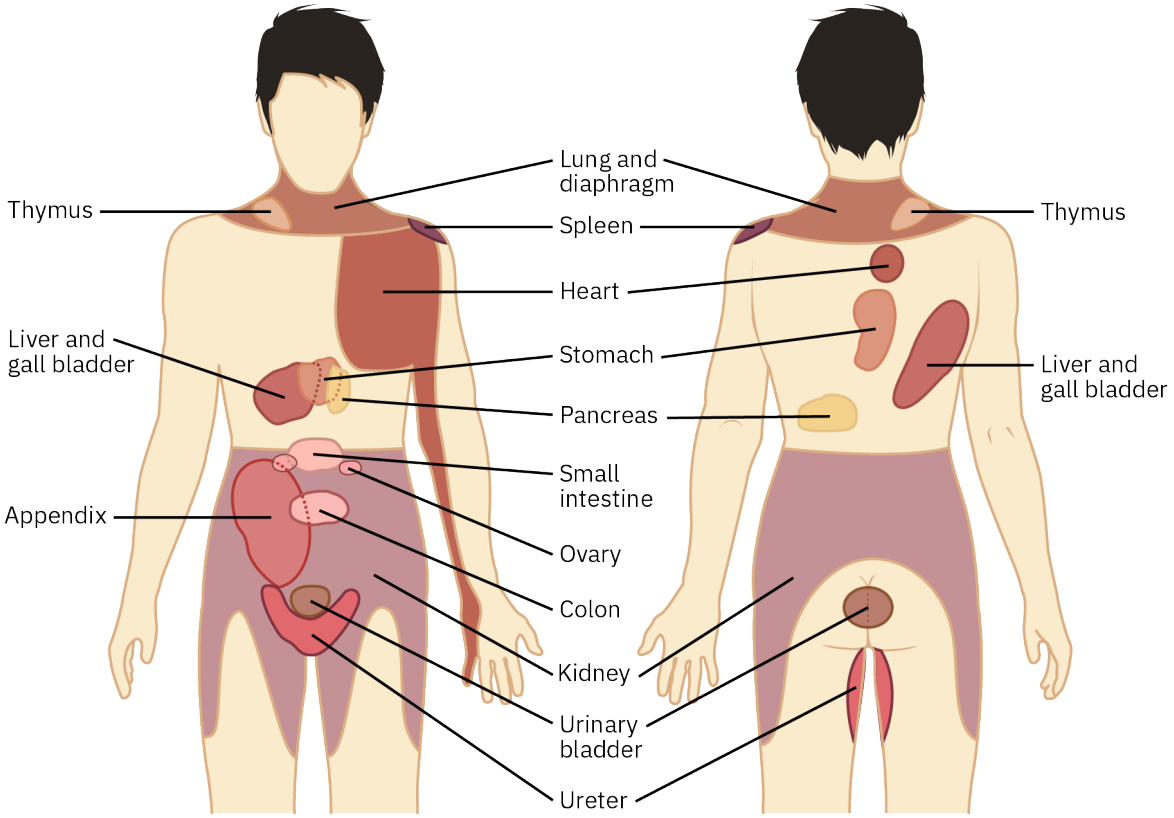


FIGURE 14.2 This illustration of referred pain maps visceral sensations to specific regions of the body. Some sensations are felt locally, whereas others are perceived as affecting areas quite distant from the involved organ. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Pain can also be characterized based on its intensity, such as by describing it as mild, moderate, or severe or rating it on a scale from 0 to 10, with 0 being no pain and 10 being the worst pain imaginable. These types of scales may not be appropriate when clients do not understand the question or cannot communicate their pain. In cases such as these, other tools are available. For instance, the nurse can display drawings of different faces expressing various levels of pain and ask the client to point to the face that best represents what they are experiencing.

Health care professionals also assess clients for physical signs of pain, which can be indicated by facial expressions, muscle tension, and body movements. Another important way to assess pain is to observe or ask about any functional impairments. It is useful to know what the client is functionally capable or incapable of doing—such as going to work, gardening, or playing with their children—and how these abilities change with pain and pain treatment. Generally, when a client's pain status improves, they should be able to do more of the things they wish to do. This provides more objective evidence than relying solely on client self-reporting.

Nurses are a critical link in the chain of appropriate pain management. They are frequently the health care professionals on the front line in assessing pain, administering pain medication, and monitoring for pain relief and any adverse effects the client may develop. It is critical for nurses to have a solid understanding of what pain is and how it may present differently in a variety of client populations such as children, older adults, and individuals from various ethnic and racial backgrounds. Cultural values and beliefs as well as individual differences can frequently affect how clients will talk about and show their pain, so it is important for nurses to be open-minded to the fact that pain is a subjective experience. Some people may live with a great deal of chronic pain but are stoic and do not exhibit outward signs of it. All individuals are equally deserving of adequate pain management, and nurses should advocate for their clients to ensure they receive the care they deserve.

LINK TO LEARNING

The Wong–Baker FACES Pain Rating Scale (https://openstax.org/r/wongbakerfaces)

The Wong–Baker FACES pain rating scale uses pictures to illustrate different severities of pain. It is especially useful when the client is too young to understand a pain-scale question or when a language barrier exists.

Pathophysiology of Pain

Nociception is the term used to describe the processing of noxious stimuli by both the peripheral and central nervous systems. Pain is the client's subjective experience of this nociception. Nociception is a complex process that involves five steps: transduction, conduction, transmission, modulation, and perception.

Transduction is the first step leading to the sensation of pain and begins with activation of specialized nerves known as **nociceptors**. Activation of these nociceptors can arise from a variety of stimuli, including direct tissue injury, extremes in temperature, and certain chemicals. Upon exposure to one of these stimuli, several types of small proteins called **cytokines** are released, which sensitize and activate the nociceptors. **Conduction** and **transmission** occur when the nociceptors are activated and turn a chemical signal into an action potential, which transmits the stimuli to the spinal column to eventually be received by the brain. **Modulation** controls how strong a painful signal will be when the brain receives it. Pain signals can be made more intense by substances such as **substance P**. Conversely, painful signals can be inhibited by substances such as the body's own natural opioids (enkephalins and beta-endorphins). The first four steps of nociception culminate in **perception** of pain by the brain. At this point, the individual experiences the subjective sensation of pain and can respond to it, such as by pulling their hand away from a hot surface.

Another major player in nociception is the immune system, which is activated when tissue is injured. Once inflammatory cytokines are released, the immune system is signaled to start recruiting immune cells, such as macrophages and neutrophils, to the site of injury. A complex cascade of chemical signaling is set in motion, including activation of the **cyclooxygenase** pathway, which leads to the characteristic hallmarks of inflammation: swelling, redness, and heightened sensations of pain.

Pain Threshold

The **pain threshold** is the point at which someone perceives a stimulus to be painful. It is highly variable and unique

to each person. Individuals can have different pain thresholds for a variety of reasons, including differences in genetic makeup, psychosocial support, and the neurochemicals that affect the modulation step of nociception, to name a few. The pain threshold can be affected by the use of nonpharmacologic strategies, including distraction techniques (e.g., meditation or listening to music), and pharmacologic agents such as nonopioid analgesics and opioid agonists.

SPECIAL CONSIDERATIONS

Pain in Various Populations

It is important to consider how biases may play a role in pain assessment of clients from various racial, ethnic, and social backgrounds. Researchers have found that health care providers often carry implicit biases that may cause them to underestimate pain in clients due to false perceptions of physiologic differences between people of different ethnicities. These biases can lead to undertreatment of these clients and cause unnecessary pain and suffering. In addition, clients driven to self-medicate because of untreated pain may be at risk for substance misuse and addiction.

One example of such bias is that Black clients often have their pain underestimated and undertreated due to a variety of false beliefs about physiologic differences between different racial groups. This is why education of health care professionals at all levels is necessary to root out these false assumptions.

(Source: Schoenthaler & Williams, 2022)

14.2 Nonopioid Analgesics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 14.2.1 Identify the characteristics of nonopioid analgesic drugs used to treat pain.
- 14.2.2 Explain the indications, actions, adverse reactions, and contraindications of nonopioid analgesic drugs used to treat pain.
- 14.2.3 Describe the nursing implications of nonopioid analgesic drugs used to treat pain.
- 14.2.4 Explain the client education related to nonopioid analgesic drugs used to treat pain.

A **nonopioid analgesic** refers to any pharmacologic agent that treats the symptoms of pain and does not involve activation of opioid receptors. These agents generally work by inhibiting cyclooxygenase (COX), a major pro-inflammatory enzyme that causes many signs and symptoms of inflammation, including redness, swelling, and sensitization of nociceptors, thereby increasing the transmission of painful signals to the brain. COX causes this increase in inflammation and pain by increasing the production of cytokines such as prostaglandins, prostacyclin, and thromboxane. It is also partly responsible for the pyrexia that occurs with infection, which is why many nonopioid analgesics that block the activity of COX also work as **antipyretics** to reduce fever.

Cyclooxygenase has two major isoforms: COX-1 and COX-2. COX-1 helps with normal homeostatic functions in the body, including maintaining normal platelet and renal functions. It also is important for producing prostaglandins that stimulate production of the mucosal barrier that protects the stomach from its own acids. If COX-1 is inhibited through the actions of medications such as glucocorticoids or nonsteroidal anti-inflammatory drugs (NSAIDs), this protective barrier can erode, which is a major cause of peptic ulcers. COX-2 is responsible for much of the inflammation and pain brought about by tissue injury.

Other nonopioid analgesics may serve as adjunctive agents for treating neuropathic sources of pain. These include antidepressant drugs (e.g., duloxetine, amitriptyline), antiseizure drugs (e.g., carbamazepine, pregabalin), and local anesthetics (e.g., lidocaine and bupivacaine). These are useful because they target the abnormal neuronal function that is the source of neuropathic pain. These medications are covered in their respective chapters, and health care professionals should keep these additional tools in mind to ensure adequate management of this type of pain.

Acetaminophen

Acetaminophen is a common over-the-counter nonopioid analgesic. It is one of the most popular analgesics due to its low cost, efficacy in treating mild to moderate pain, and excellent safety profile when used within the

recommended dosages. Acetaminophen's complete mechanism of action to relieve pain is not currently known. Some experts theorize that it inhibits COX in the central nervous system (CNS), providing analgesic and antipyretic actions, but notably it does not inhibit COX peripherally, meaning it has no anti-inflammatory action as compared with other nonopioid analgesics.

Acetaminophen comes in a variety of dosage forms, including intravenous and rectal options, to aid clients who cannot take medications by mouth. Acetaminophen is commonly found in combination products with opioid agonists, antihistamines, and medications for coughs and colds. Because acetaminophen is present in so many products, and because its overuse can lead to serious adverse events, nurses must be alert for all sources of acetaminophen that clients may be taking.

CLINICAL TIP

Check for All Sources of Acetaminophen

Many over-the-counter and prescription medications include acetaminophen, including many cough and cold products. Clients should be aware that they need to count all sources of acetaminophen to ensure they do not exceed the limit of 4000 mg per 24 hours and put themselves at risk for liver injury.

Aspirin, Ibuprofen, and Naproxen Sodium

Aspirin, ibuprofen, and naproxen sodium are classified as **nonsteroidal anti-inflammatory drugs (NSAIDs)**. This classification means they possess analgesic, antipyretic, and anti-inflammatory actions without belonging to the group of medications known as the glucocorticoids (e.g., prednisone and dexamethasone, which are discussed in Introduction to the Immune System and the Inflammatory Response). NSAIDs are often preferred over glucocorticoids as anti-inflammatory agents because they cause fewer adverse drug reactions such as hyperglycemia, hypertension, and increased risk for infection. NSAIDs work by inhibiting the enzyme COX centrally and in peripheral tissues to decrease inflammation and reduce pain. NSAIDs are also very popular analgesics because they are readily available over the counter.

Aspirin is notable for its antiplatelet actions, so it can be used during myocardial infarctions to aid in maintaining coronary blood flow by inhibiting platelet aggregation. (See Cardiac Emergency and Shock Drugs for more about aspirin's use in cardiovascular emergencies.) The reason for aspirin's unique actions is that it is an irreversible inhibitor of COX in platelets, preventing them from aggregating and initiating the clotting cascade. Aspirin's irreversible inhibition of COX means that platelets are affected for their entire lifetime, which is approximately 7–10 days. Nurses should instruct clients taking blood thinners (e.g., warfarin, apixaban) to be cautious about using aspirin to treat pain because of increased risk for bleeding and bruising.

SAFETY ALERT

NSAIDs

Clients reporting severe abdominal pain, dark tarry stools, or vomiting or coughing up of blood should stop using any NSAIDs immediately and be assessed by a health care provider for possible stomach ulcers.

Tramadol

Tramadol is a partial opioid receptor agonist and inhibitor of reuptake of the neurotransmitters norepinephrine and serotonin. These characteristics make tramadol a potential analgesic option for clients with neuropathic pain because they benefit from both the partial opioid effect and the pain-modulating effects of increased norepinephrine and serotonin. However, due to its actions at the opioid receptors, tramadol has been linked to cases of misuse and addiction, leading the Drug Enforcement Administration (DEA) to categorize tramadol as a Schedule IV medication (CIV). The DEA scheduling of a medication puts certain restrictions on who can prescribe the medication and how much of the medication can be prescribed at a time.

Table 14.1 lists common nonopioid analgesics and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Acetaminophen (Tylenol)	*Pain and/or fever:* *Adults:* 325–650 mg orally every 4–6 hours as needed; maximum dose: 4000 mg/day. *Children:* 10–15 mg/kg/dose orally every 4–6 hours as needed; maximum dose: 75 mg/kg/day, not to exceed 4000 mg/day.
Aspirin	*Pain and/or fever:* *Adults:* 325–1000 mg orally every 4–6 hours as needed; usual maximum dose is 4000 mg/day. *Secondary prevention of atherosclerotic cardiovascular disease:* *Adults:* 75–325 mg once daily.
Ibuprofen (Advil, Motrin)	*Pain and/or fever:* *Adults:* 200–800 mg orally every 4–8 hours as needed; maximum dose: 3200 mg/day. *Children:* 10 mg/kg/dose orally every 6–8 hours; maximum dose: 600 mg/dose, not to exceed 2400 mg/day.
Naproxen sodium (Aleve, Naprosyn)	*Pain and/or fever:* *Adults:* 200–400 mg orally, followed by 200 mg every 8–12 hours as needed; maximum dose: 600 mg/day.
Tramadol (Ultram)	*Pain:* *Adults:* 25–100 mg orally every 6 hours as needed; maximum dose: 400 mg/day.

TABLE 14.1 Drug Emphasis Table: Nonopioid Analgesics (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Nonopioid analgesics as a class are relatively safe to use for many clients but do carry some notable adverse effects in susceptible individuals. Acetaminophen is a preferred analgesic for mild to moderate pain because it has relatively few adverse effects, but it must not be taken in amounts greater than those recommended by the drug's manufacturers. This limit is 4000 mg per 24 hours; taking acetaminophen in doses beyond that increases the chances of developing potentially fatal **hepatotoxicity**. Clients with a history of liver disease will have lower recommended dosages because they are at greater risk for liver injury when using acetaminophen. Hepatotoxicity from acetaminophen can present as nausea, fatigue, and jaundice (yellowish skin and sclera) and may require antidotal therapy with the drug n-acetylcysteine to help prevent further liver injury.

NSAIDs such as aspirin, ibuprofen, and naproxen sodium are known to increase the risk for bleeding and bruising and can cause kidney injury in older adults and in clients with a history of chronic kidney disease. NSAIDs taken at high doses for long periods of time can also potentially cause stomach ulcers that can progress to bleeding and perforation by eroding the protective stomach lining over time.

Due to its opioid receptor activity, tramadol can cause CNS and respiratory depression in overdose or when mixed with other CNS depressants such as alcohol. It is associated with risk for problematic use and addiction, and individuals with a history of substance use disorder should avoid it. Tramadol can lower the seizure threshold and should be used with caution in clients with a history of seizure disorder.

NSAIDs carry a risk for asthma exacerbations in clients with a history of aspirin-induced asthma. Aspirin should be avoided in children younger than 16 years old with a recent history of viral illness because the medication may cause a potentially fatal condition called **Reye's syndrome**.

All of these agents should be avoided in clients with a known allergy to the individual agents or any of their components.

Table 14.2 is a drug prototype table for nonopioid analgesics featuring ibuprofen. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nonsteroidal anti-inflammatory drug (NSAID) **Mechanism of Action** Inhibits the enzyme cyclooxygenase to decrease the production of inflammatory cytokines and thereby reduce inflammation and pain	**Drug Dosage** *Adults:* 200–800 mg orally every 4–8 hours as needed; maximum dose: 3200 mg/day. *Children:* 10 mg/kg/dose orally every 6–8 hours; maximum dose: 600 mg/dose, not to exceed 2400 mg/day.
Indications Temporarily relieves minor aches and pains Temporarily reduces fever **Therapeutic Effects** Reduces fever Reduces inflammation Decreases pain	**Drug Interactions** Angiotensin II receptor blockers (e.g., candesartan) Angiotensin-converting enzyme (ACE) inhibitors (e.g., lisinopril) Lithium Warfarin **Food Interactions** No significant interactions
Adverse Effects Decreased hemoglobin Edema Skin rash Abdominal cramps Constipation Diarrhea Nausea Gastric ulcer Heartburn Dizziness	**Contraindications** Hypersensitivity Aspirin-sensitive asthma Allergic reaction to aspirin Caution: Asthma Hepatic impairment Renal impairment Bariatric surgery

TABLE 14.2 **Drug Prototype Table: Ibuprofen** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking a nonopioid analgesic:

- Assess the client for pain by using a pain scale before and 15–20 minutes after a dose of a nonopioid analgesic to determine its efficacy.
- Ensure that the client does not receive more than the recommended amount of acetaminophen in 24 hours.
- Check for any contraindications, allergies, or potential drug interactions before beginning therapy with a nonopioid analgesic.
- Ask the client when they last used an analgesic medication.
- Ask the client about any types of nonpharmacologic pain treatment they may be using, such as ice, stretching, or heat/cold therapy.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a nonopioid analgesic should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider about any signs of bleeding, including black tarry stools, coffee-ground emesis, or blood-streaked sputum.
- Alert their health care provider that they are taking this medication, including the dose and frequency.
- Avoid drinking alcohol while using acetaminophen.

- Take the drug with food if it causes upset stomach.
- Take a missed dose as soon as they remember it; however, they should *not* take double doses.
- Contact their health care provider for further advice if pain persists longer than 3 days.

FDA BLACK BOX WARNING

Nonopioid Analgesics

Acetaminophen has been associated with cases of acute liver failure, at times resulting in death or the need for liver transplantation.

NSAIDs increase the risk for serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use.

NSAIDs increase the risk for serious gastrointestinal adverse events, including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Older adults and individuals with a prior history of peptic ulcer disease or gastrointestinal bleeding are at greater risk for serious gastrointestinal events.

UNFOLDING CASE STUDY

Part A

Read the following clinical scenario to answer the questions that follow. This case study will evolve throughout the chapter.

Maria Vega is a 63-year-old client who presents to her health care provider's office with reports of abdominal pain, diarrhea that is occasionally black and tarry in appearance, and dizziness.

History

Coronary artery disease
Osteoarthritis (both knees and hips are affected)

Current Medications

Aspirin 81 mg orally once daily
Metoprolol 50 mg orally twice daily
Over-the-counter ibuprofen 400 mg orally every 4–6 hours as needed for joint pain

Vital Signs		Physical Examination
Temperature:	98.8°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; no peripheral edema noted bilaterally; S1, S2 auscultated, rhythm regular • *Respiratory:* Lungs clear to auscultation bilaterally • *GI:* Abdomen soft, generalized tenderness, nondistended; normal bowel sounds auscultated in all four quadrants • *GU:* Reports normal urine output • *Neurologic:* Within normal limits • *Integumentary:* No wounds noted; skin appropriate for age
Blood pressure:	126/86 mm Hg	
Heart rate:	74 beats/min	
Respiratory rate:	16 breaths/min	
Oxygen saturation:	97% on room air	
Height:	5'3"	
Weight:	122 lb	

TABLE 14.3

TABLE 14.3

1. Based on the information above, what is the most important question for the nurse to ask Maria?
    a. "How long have you been taking aspirin?"
    b. "How many stools have you had today?"
    c. "How much ibuprofen do you take each day?"
    d. "Have you lost any weight in the last month?"

2. The nurse determines that the client is taking 2 or 3 200 mg tablets nine times daily to control her arthritic pain. Which instruction should the nurse give the client?
    a. "This dose is too low to effectively relieve arthritis pain."
    b. "This dose is appropriate for arthritis pain."
    c. "This dose may cause respiratory depression."
    d. "This dose is too high and can cause gastric bleeding."

14.3 Opioid Agonists and Antagonists

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 14.3.1 Identify the characteristics of opioid agonist and antagonist drugs used to treat pain.
- 14.3.2 Explain the indications, actions, adverse reactions, and contraindications of opioid agonist and antagonist drugs used to treat pain.
- 14.3.3 Describe nursing implications of opioid agonist and antagonist drugs used to treat pain.
- 14.3.4 Explain the client education related to opioid agonist and antagonist drugs used to treat pain.

Opioid Agonists

Opioid agonists have been in use for thousands of years. Opioids originated from the opium poppy, *Papaver somniferum*, from which naturally occurring opioids such as heroin, codeine, and morphine are derived. Since the discovery of the potent analgesic effects of these medications, other opioids have been developed, including hydrocodone and oxycodone. The term *opiate* strictly refers to agents that come from the opium poppy (e.g., heroin, morphine), but is often used interchangeably with the term *opioid*. Opioid agonists are some of the most potent analgesics available and are used for treatment of moderate to severe pain. However, opioids carry a risk for misuse and addiction that has led to one of the most notable public health crises to date, the opioid epidemic. Because of these risks, the DEA categorizes all opioids as controlled substances. Most opioids fall under the strict categorization of Schedule II (CII), meaning they have an acceptable medical use but are associated with a high risk for misuse and addiction.

Opioids produce many of their desired therapeutic effects and potentially life-threatening adverse effects via the opioid receptors, including the mu, delta, and kappa receptors. When activated, these receptors located throughout the CNS help modulate painful signals from peripheral tissues to alter pain perception and heighten the pain threshold. These same receptors are also known to cause many of the notable adverse effects of opioids, including the CNS and respiratory depression that can be seen in overdose. Opioid agonists also suppress the cough receptors in the brain and can be used as cough suppressants. However, due to the risk for misuse and addiction, opioid agonists are usually considered last-line treatments for cough.

Codeine

Codeine is one of the naturally occurring opioids derived from the opium poppy. It is most often given orally for mild to moderate pain. For codeine to be effective, it must be converted to morphine in the liver via the enzyme **cytochrome P450 2D6** (CYP2D6). Because individuals may produce more or less CYP2D6, clients receiving codeine may experience unpredictable therapeutic and adverse effects. Clients who produce too little CYP2D6 (slow metabolizers) do not convert enough codeine into morphine and thus may not receive adequate analgesia. Clients producing many copies of CYP2D6 (rapid metabolizers) may convert too much codeine into morphine, causing enhanced analgesic effects and a greater risk for life-threatening respiratory depression. Due to this variability in client metabolism and potential risks, the American Academy of Pediatrics does not currently recommend codeine for use in children (Silva et al., 2021). Similarly, codeine should be used with caution in older clients.

Fentanyl

Fentanyl is a potent synthetic opioid that is frequently used intravenously to treat severe pain related to trauma or surgery. It is also available in patches to help provide long-lasting analgesia in clients with chronic pain conditions. Fentanyl is considered a synthetic opioid because it shares no chemical resemblance to naturally occurring opioids such as morphine, which means it can be a safe alternative for clients who have a documented morphine allergy. Because of its potency, fentanyl is often used by clients with opioid use disorders, and it has become a major contributor to opioid-related deaths in the past several years (National Institute on Drug Abuse, 2023).

Hydromorphone

Hydromorphone is a semisynthetic derivative of morphine, meaning it shares some chemical structure similarities with naturally occurring opioids. It is a potent analgesic and is most frequently used for cases of moderate to severe pain. Hydromorphone is available in both intravenous and oral forms, so it is frequently used for clients with severe pain both in and outside the hospital setting.

Meperidine

Meperidine is a synthetic opioid that is not routinely used as an analgesic. This is because it produces a toxic metabolite that can accumulate in older adults with poor renal function, leading to risk for delirium and seizures. Instead, the most common use for meperidine is to interrupt the severe shivering with chills (also known as rigors) that may occur postoperatively in clients who received general anesthesia.

Methadone

Methadone is a synthetic opioid that is most frequently used to treat opioid use disorders. Because of its long half-life, up to 59 hours, it persists in the body longer than many other opioids. This long half-life helps prevent the opioid **withdrawal** symptoms that can occur when individuals stop using opioids entirely. Methadone's long half-life also means that it has utility in providing long-lasting pain relief in clients with chronic pain. In addition, it has some efficacy in treating neuropathic pain because it can block the reuptake of the neurotransmitters norepinephrine and serotonin, which helps reduce painful signals from being transmitted to the brain.

Morphine

Morphine is a naturally occurring opioid that has been in widespread use since its discovery in the 1800s. It is considered to be the prototypical opioid to which all others are compared. It is used to treat both acute and chronic types of pain and is available in a wide variety of dosage forms, including intravenous and oral options. Oral forms come in immediate and extended-release formulations, making morphine suitable for breakthrough and around-the-clock types of pain. Because of its high degree of efficacy, morphine is used for moderate to severe pain.

Oxycodone

Oxycodone is a semisynthetic opioid commonly used orally to treat moderate to severe pain. It is frequently used because of its favorable side effect profile compared with other agents such as morphine (for instance, oxycodone causes less itching).

Oxycodone comes in a variety of dosage forms, including immediate- and extended-released preparations, making it useful for acute and chronic pain therapy in outpatient settings. The extended-release formulation, sold under the brand names OxyContin and Xtampza ER, is used to provide around-the-clock pain relief. Clients with chronic pain often need long-acting medications for their basal levels of pain (i.e., the baseline level of pain that is always present) as well as short-acting agents for breakthrough episodes of pain (i.e., pain above the basal level brought on by injury or activity).

Oxycodone is often coformulated with acetaminophen, which nurses should consider when totaling a client's total daily acetaminophen intake.

Table 14.4 lists common opioid agonists and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Codeine	*Pain:* 15–60 mg orally every 4 hours as needed; maximum dose: 360 mg/day.
Fentanyl (Sublimaze, Duragesic, Actiq)	*Acute severe pain:* 25–50 mcg every 30–60 minutes intravenously (IV) or intramuscularly as needed. *Chronic pain:* Transdermal patch; initial fentanyl transdermal dose (25–100 mcg/hour) based on prior 24-hour oral morphine requirement.
Hydromorphone (Dilaudid)	*Acute pain:* *Intravenous:* 0.2–1 mg IV every 2–3 hours as needed. *Oral:* 2–4 mg orally every 4–6 hours as needed.
Meperidine (Demerol)	*Acute pain:* 50–150 mg intramuscularly/subcutaneously every 3–4 hours as needed; maximum dose: 600 mg/day.
Methadone (Dolophine)	*Chronic pain:* Dosing is individualized; typical dose: 2.5–5 mg orally every 8–12 hours.
Morphine (Duramorph, MS Contin)	*Acute pain:* *Intravenous:* 0.1–0.2 mg/kg IV every 1–4 hours as needed. *Oral:* 15–30 mg orally every 4 hours as needed.
Oxycodone (Roxicodone, OxyContin)	*Immediate-release for acute pain:* 5–15 mg orally every 4–6 hours as needed. *Extended-release for chronic pain*: 10 mg orally every 12 hours.

TABLE 14.4 **Drug Emphasis Table: Opioid Agonists** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of opioid therapy can range from general gastrointestinal upset to life-threatening respiratory depression. The most common are gastrointestinal effects, including nausea, vomiting, and constipation. Nearly all clients receiving chronic opioid therapy will develop constipation, so nurses should assess for this to help determine which type of constipation treatment (laxatives, stool softeners, stimulants, fiber supplements) the client needs to ensure regular bowel movements. A handy mnemonic for adverse effects is NARCS U: nausea, acute toxicity/addiction, respiratory depression, constipation, sedation, and urinary retention.

Morphine is known to cause significant histamine release in susceptible clients and may manifest as flushing, pruritis, and hypotension. This situation is normally managed by using an alternative opioid that does not cause histamine release (e.g., hydromorphone or oxycodone) or treating the client with an antihistamine such as diphenhydramine to combat the actions of histamine release. (Antihistamines are discussed in Upper Respiratory Disorder Drugs.)

In overdose or in combination with other CNS depressants (e.g., benzodiazepines, muscle relaxants, alcohol), the most dangerous effects seen with opioids include CNS and respiratory depression. The individual may appear sedated or can be completely unresponsive, and their breathing may be slow, shallow, or absent. These signs constitute a medical emergency and necessitate the use of an opioid antagonist such as naloxone hydrochloride (discussed in the following section) along with the response of emergency medical services.

Opioids should be avoided in clients with any known hypersensitivities to them or to any of their constituent components. Clients with documented allergies to naturally occurring opioids such as morphine are generally able to safely receive synthetic opioids such as fentanyl because the chemical structures differ enough that there is low cross-sensitivity between these agents. Clients with significant respiratory depression or gastrointestinal obstruction should also avoid opioids because these conditions can worsen when opioids are present in the body.

CLINICAL TIP

Assess for Constipation

Opioid agonists are well known to cause significant constipation when taken chronically. Constipation can cause or worsen abdominal pain and may distress the client. The nurse should recommend to most clients that they

consume more water and fiber in their diet. Many clients will need to use laxatives such as senna and docusate to ensure normal stooling habits.

Table 14.5 is a drug prototype table for opioid agonists featuring morphine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Opioid analgesic **Mechanism of Action** Activates opioid receptors to modulate and reduce incoming painful signals to reduce pain perception	**Drug Dosage** *Intravenous:* 0.1–0.2 mg/kg IV every 1–4 hours as needed. *Oral:* 15–30 mg orally every 4 hours as needed.
Indications Moderate to severe pain **Therapeutic Effects** Reduced pain perception	**Drug Interactions** Alprazolam Diphenhydramine Cyclobenzaprine **Food Interactions** Alcohol
Adverse Effects Edema Flushing Hypotension Tachycardia Rash Central nervous system depression Respiratory depression Dizziness Drowsiness Euphoria Miosis Blurred vision	**Contraindications** Hypersensitivity Respiratory depression Severe asthma Paralytic ileus Caution: CNS depression Hypotension Abdominal conditions Hepatic impairment Renal impairment Thyroid dysfunction Mental health conditions

TABLE 14.5 **Drug Prototype Table: Morphine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking an opioid:

- Assess the client's pain before and after administering an opioid to determine its efficacy in treating the client's pain.
- Watch for adverse effects, including sedation, ataxia, slurred speech, and shallow breathing, which could require the use of antidotal therapy or respiratory support.
- With chronic use of opioids, ask about the client's bowel movements because constipation is very common with these medications and could be a source of abdominal pain.
- Ensure that naloxone is readily available in the event of opioid toxicity or overdose.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

SAFETY ALERT

Opioid Agonists

Although respiratory depression is rare when opioid agonists are used in therapeutic doses, nurses should instruct clients not to mix opioids with other CNS depressants, including sedatives, alcohol, and muscle

relaxants, because this interaction will increase the risk for potentially fatal respiratory failure. Naloxone hydrochloride should be coprescribed to clients who are at greater risk for opioid overdose.

CLIENT TEACHING GUIDELINES

The client taking an opioid agonist should:

- Alert their health care provider before starting opioid agonist therapy if they have any breathing difficulties, asthma, or sleep apnea.
- Alert their health care provider about any signs or symptoms of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Take the lowest dose needed, if prescribed as as-needed (prn) use, to control pain to reduce the risk of dependence.
- Alert all health care providers that they are taking opioids, including the dose and frequency.
- Take a missed dose as soon as they remember it; however, they should *not* take double doses.
- Keep all medication out of the reach of children and pets.

The client taking an opioid agonist *should not:*

- Crush or chew the product if taking an extended-release drug.
- Mix opioids with other CNS depressants, including sedatives, alcohol, and muscle relaxants, because their interaction increases the risk for potentially fatal respiratory failure.
- Share opioids with family or friends because this practice can lead to harm or even death.

FDA BLACK BOX WARNING

Opioid Agonists

Opioid agonists expose clients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each client's risk prior to prescribing and reassess all clients regularly for the development of these behaviors and conditions.

Serious, life-threatening, or fatal respiratory depression may occur with use of opioid agonists. Monitor for respiratory depression, especially during initiation of opioid agonists or following a dose increase. To reduce the risk of respiratory depression, proper dosing and titration of opioid agonists is essential.

Accidental ingestion of opioid agonists, especially by children, can be fatal.

Concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of tramadol and benzodiazepines or other CNS depressants for use in clients for whom alternative treatment options are inadequate. Limit treatment to the minimum effective dosages and durations. Follow clients for signs and symptoms of respiratory depression and sedation.

Prolonged use of opioid agonists during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant client, advise the client of the risk for neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Tolerance and Addiction

Tolerance and addiction are two important topics concerning the use of opioid medications. Clients and health care professionals can misunderstand the definitions of these terms and how likely the conditions are to occur. It is important for nurses to understand these terms and how they apply to clients using opioids.

Tolerance

Tolerance is a phenomenon that occurs in clients taking opioid agonists chronically. As the body adapts to the presence of the drug, the client will become accustomed to some of the side effects, including sedation, and it may appear as if the dose that previously treated the client's pain is no longer adequate. Therefore, the opioid dose may need to be increased to treat the client's pain adequately. In fact, clients can develop so much tolerance that the dose that is appropriate for them would be potentially dangerous to someone who has never taken an opioid agonist. This tolerance is a normal phenomenon that occurs in nearly all clients receiving chronic opioid agonists and should not be confused with addiction.

Clients who have developed a significant amount of tolerance to the effects of opioids are at risk for developing withdrawal symptoms when the medication is discontinued. Opioid withdrawal can be extremely distressing to the client and may result in agitation, sweating, diarrhea, and severe dysphoria. Fortunately, opioid agonist withdrawal is not associated with significant mortality, in contrast to withdrawal from CNS depressants such as alcohol or benzodiazepines, which can cause seizures and is associated with greater mortality risk.

Addiction

Opioid **addiction** (also called **opioid use disorder**) is a condition characterized by compulsive use of opioids, increased opioid tolerance, and withdrawal symptoms if the client does not continue taking an opioid agonist. This compulsion can be so strong in susceptible individuals that they will continue using opioids despite the known physical, financial, and social harms that it may be causing. It is estimated that in the United States, 2.1 million individuals have opioid use disorders and 47,000 deaths are attributable to opioid agonists each year (Wilson et al., 2020).

Addiction typically occurs as a result of dopamine release in the reward pathway of the brain, also known as the dopaminergic pathway. This causes an intense euphoria that often leaves the client wanting more opioids to feel that same elation repeatedly. Risk factors for developing an opioid use disorder include genetic and environmental factors. Clients with a history of certain mental health disorders, such as post-traumatic stress disorder and depression, have been shown to be at risk for various substance use disorders as well (National Institute on Drug Abuse, 2022).

It is important to determine how clients are obtaining their opioids because not all opioids are obtained legally. Nurses also should ask about the illicit use of opioids, such as heroin, that may not be documented in the medical chart.

Not all clients who use opioids will develop opioid use disorders; however, this possibility is a concern for many clients who may have pain but refuse all opioids based on the small risk of addiction. It is important to counsel clients about the differences between tolerance and addiction to ensure they feel comfortable getting the best care that is right for them. Tolerance and physical dependence will occur in nearly all clients receiving chronic opioid therapy, but only some will go on to develop an opioid use disorder.

UNFOLDING CASE STUDY

Part B

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up to Unfolding Case Study Part A.

Two months after the last encounter, Maria Vega presents to the emergency department following a fall at home. She rates her right ankle pain as 6/10 on a 0- to 10-point pain scale. She is diagnosed with a right ankle fracture.

History

Coronary artery disease
Osteoarthritis

Current Medications

Aspirin 81 mg orally once daily

Metoprolol 50 mg orally twice daily
Over-the-counter ibuprofen 400 mg orally every 4–6 hours as needed for joint pain

Vital Signs		Physical Examination
Temperature:	97.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; no peripheral edema noted bilaterally; S1, S2 auscultated; rhythm regular • *Respiratory:* Lung clear to auscultation bilaterally • *GI*: Abdomen soft, nontender, nondistended; normal bowel sounds auscultated in all four quadrants • *GU:* Reports normal urine output • *Neurologic*: Within normal limits • *Integumentary*: No wounds noted; skin appropriate for age • *Extremities:* Right ankle in a splint, toes are pink; dorsalis pedis pulses strong bilaterally; able to feel light touch and wiggle toes of right foot
Blood pressure:	146/66 mm Hg	
Heart rate:	93 beats/ min	
Respiratory rate:	18 breaths/ min	
Oxygen saturation:	96% on room air	
Height:	5'3"	
Weight:	122 lb	

TABLE 14.6

3. Based on the information above, which medication does the nurse anticipate the provider will order for the client's pain?
   a. Acetaminophen
   b. Ibuprofen
   c. Hydromorphone
   d. Meperidine

4. The health care provider prescribes hydromorphone for the client's ankle pain. Which information will the nurse give the client about this drug?
   a. "Do not drink alcohol while you're taking this medication."
   b. "Reduce your fiber intake while taking this medication."
   c. "Your heart rate might slow down when you're taking this medication."
   d. "This medication might lower your blood pressure."

Opioid Antagonists

Opioid analgesics are extremely effective when used to manage moderate to severe forms of pain but can cause potentially life-threatening CNS and respiratory depression when the recommended dosage is exceeded or when individuals use them along with other CNS depressants (e.g., alcohol). It is critical that agents are available to reverse the effects of opioids to avoid severe injury and potential death. This section will cover these opioid antagonists.

Naloxone Hydrochloride

Naloxone hydrochloride is an opioid receptor antagonist that is used as an antidote in people experiencing signs and symptoms of opioid agonist overdose, including severe CNS and respiratory depression. Overdose may present as shallow or absent breathing, and the person may be unresponsive to any type of stimuli. Naloxone works by blocking the opioid receptors, thus causing a rapid reversal of opioid agonist effects. Because the individual will be too sedated to administer the medication themselves, it will often be given by emergency medical services, law enforcement officers, or bystanders with access to naloxone. Naloxone can be given intravenously, intramuscularly, or intranasally.

Importantly, naloxone has a duration of action of only approximately 20–30 minutes. This short duration means the individual may resedate because many opioids have a longer duration of action than naloxone does. This is why it is critical that those who respond to naloxone receive medical care as quickly as possible to prevent delaying more definitive therapy. The only major adverse effect of naloxone is that it can induce severe opioid withdrawal in

individuals who chronically use opioids; they may become very agitated, develop diarrhea, and experience intense dysphoria. To avoid these consequences of sudden withdrawal, smaller doses may be administered in quick succession until the individual is able to breathe on their own.

Naltrexone Hydrochloride

Naltrexone hydrochloride is an opioid receptor antagonist. It is not often given for emergency reversal of opioid intoxication but is instead used for clients who want to abstain from opioid use. It is orally bioavailable, and when a client has been taking it orally, it will blunt the effects of opioids if the client relapses and begins to use opioids again. Long-acting formulations of naltrexone can also be administered intramuscularly every 4 weeks to ensure client compliance during this period. Adverse effects of naltrexone are similar to those of naloxone in that it can induce opioid withdrawal in clients who are actively using opioids.

Recent research suggests that naltrexone can be used in combination with other medications to treat a variety of addictive conditions, such as eating disorders (Stancil et al., 2019). See Substance Use Disorder Treatment Drugs for more information on naltrexone.

Nalbuphine Hydrochloride

Nalbuphine is a mixed opioid agonist/antagonist. On its own, it can serve as an alternative to other opioid agonists when treating pain. At lower doses, it acts as an antagonist and can reverse the depressant effects of other opioid agonists.

Table 14.7 lists common opioid antagonists and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Naloxone hydrochloride (Narcan)	*Opioid overdose (known or suspected):* 0.4–2 mg as needed. *Intranasal spray:* 4–8 mg in one nostril every 2–3 minutes until medical assistance is available.
Naltrexone hydrochloride (Vivitrol)	*Treatment of opioid dependence:* *Oral:* 25–50 mg daily. *Intramuscular:* 380 mg every 4 weeks.
Nalbuphine hydrochloride (Nubain)	*Acute pain:* 10 mg subcutaneously/intramuscularly/IV every 3–6 hours as needed.

TABLE 14.7 Drug Emphasis Table: Opioid Antagonists (source: https://dailymed.nlm.nih.gov/dailymed/)

Table 14.8 is a drug prototype table for opioid antagonists featuring naloxone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Opioid antagonist **Mechanism of Action** Competitively antagonizes opioid receptors to reverse the depressant effects of opioids	**Drug Dosage** *Opioid overdose (known or suspected):* *IV:* 0.4–2 mg as needed. *Intranasal spray:* 4–8 mg in one nostril every 2–3 minutes until medical assistance is available.
Indications Opioid overdose **Therapeutic Effects** Reversal of opioid effects	**Drug Interactions** Opioid agonists **Food Interactions** No significant interactions
Adverse Effects Flushing Hypotension Tachycardia Diaphoresis Abdominal cramps Diarrhea Agitation Disorientation Dizziness	**Contraindications** Hypersensitivity Caution: Acute opioid withdrawal

TABLE 14.8 **Drug Prototype Table: Naloxone** (source: https://dailymed.nlm.nih.gov/dailymed/)

TRENDING TODAY

Over-the-Counter Naloxone

In March 2023, the U.S. Food and Drug Administration approved naloxone hydrochloride nasal spray to be sold over the counter to increase access to this life-saving medication (U.S. Food and Drug Administration, 2023). This change in the status of naloxone has paved the way to making it available in a variety of locations outside of pharmacies, including Internet retailers, gas stations, and grocery stores. This change is a crucial step to address the number of opioid overdose deaths that occur in the United States every year, as getting naloxone even a few minutes before emergency medical services arrive could mean the difference between life and death. A *New York Times* podcast (https://openstax.org/r/narcan) describes the importance of naloxone becoming available over the counter.

Chapter Summary

This chapter covered what pain is, how the brain perceives it, and how medications are commonly used to treat it. Because the nature of pain is subjective, different ways to assess a client's pain were explained. The concept of the pain threshold and factors that can affect it were described.

Drug classes covered in this chapter include the nonopioid analgesics, opioid agonists, and opioid antagonists. Common nonopioid analgesics include many over-the-counter medications such as acetaminophen and NSAIDs as well as tramadol. Potential serious adverse effects of opioid agonists and the risk for tolerance and addiction were explained as well as the potential for opioid antagonists to induce opioid withdrawal.

Key Terms

acute pain pain that is sudden in onset and is expected to last less than 1 month
addiction a persistent, compulsive dependence on a substance or behavior despite known harm
antipyretics medications used to treat fever
chronic pain pain persisting longer than 3 months
conduction the process of converting chemical signals into electrical signals to be carried by nerves
cyclooxygenase an enzyme responsible for the production of several inflammatory cytokines, including prostaglandins
cytochrome P450 2D6 a family of oxidative enzymes responsible for metabolizing many different drugs
cytokines proteins that regulate inflammation in immune responses
hepatotoxicity injury to the liver caused by many factors, such as a drug, environmental toxins, or radioactive exposure
modulation the process of enhancing or inhibiting a painful signal before it reaches the brain
neuropathic pain pain that originates in the peripheral or central nervous system
nociception the processing of noxious stimuli by both the peripheral and central nervous system
nociceptive pain pain that occurs because of tissue injury
nociceptors specialized nerves that respond to painful stimuli
nonopioid analgesic any analgesic that does not activate the opioid receptors to relieve pain
nonsteroidal anti-inflammatory drugs (NSAIDs) a classification of drugs that reduce inflammation by inhibiting the enzyme cyclooxygenase
opioid agonists drugs that activate opioid receptors
opioid use disorder a persistent, compulsive dependence on opioids
pain an unpleasant sensory and emotional experience associated with actual or potential tissue damage
pain threshold the point at which a stimulus is perceived as painful
perception the point at which the brain receives a painful signal
referred pain deep visceral pain that causes pain elsewhere in the body (e.g., pancreatic injury that causes back pain, myocardial infarction that causes jaw and shoulder pain)
Reye's syndrome a disorder characterized by liver and brain toxicity culminating in life-threatening neurologic symptoms, seen most often in the setting of aspirin therapy in children with a viral illness
substance P a neurotransmitter that enhances pain perception
tolerance physiologic adaptation to the effect of a drug after repeated exposure
transduction the initial activation of nociceptors
transmission the process of carrying a painful signal from the peripheral nervous system to the brain
withdrawal physiologic effects that occur after discontinuation of a drug that has been used for a prolonged period

Review Questions

1. A client presents to the clinic reporting dull, throbbing left leg pain, rated as 4/10 on a 0–10 pain scale. They have been experiencing this for the past year following a leg fracture in a car collision. The nurse determines that this client is experiencing which type of pain?
   a. Acute pain
   b. Chronic pain
   c. Neuropathic pain
   d. Severe pain

2. A client who had a cholecystectomy earlier in the day asks the nurse for pain medication for pain rated as 6/10 on a 0–10 pain rating scale. When the nurse returns with the pain medication, the client is chatting and laughing with a visitor. Which action should the nurse take?
   a. Assume that the client is not in pain
   b. Determine that the client was not rating their pain correctly
   c. Administer the pain medication
   d. Challenge the client's pain rating

3. A client with no past medical history is prescribed acetaminophen, as needed, for pain related to starting a new workout regimen. They have acetaminophen 500 mg tablets at home. The nurse instructs the client not to exceed how many tablets per day?
   a. 10
   b. 12
   c. 6
   d. 8

4. The health care provider has recommended that a client begin taking an anti-inflammatory drug to reduce the pain of osteoarthritis. Which medication does the nurse anticipate the provider will order?
   a. Tramadol
   b. Naltrexone
   c. Ibuprofen
   d. Nalbuphine

5. A 75-year-old client reports intermittent pain that ranges from 4 to 10 on a 0–10 scale. The client states that the pain started 5 years ago after they had herpes zoster (shingles). The nurse understands that this pain is classified as which of the following types?
   a. Nociceptive
   b. Neuropathic
   c. Acute
   d. Visceral

6. The nurse administers morphine intravenously to a postoperative client and returns 20 minutes later to reassess the client. The nurse observes the client taking slow and shallow breaths, and they are unresponsive to verbal and physical stimuli. The nurse activates the rapid response team and prepares to administer which medication?
   a. Tramadol
   b. Naloxone
   c. Acetaminophen
   d. Methadone

7. A nurse in an emergency department is taking a medication history on a new client. The client reports previously experiencing flushing, itching, and low blood pressure after taking an opioid for pain caused by a bone fracture but does not recall the name of the medication. The nurse suspects that the client was most likely taking which opioid?
   a. Hydromorphone
   b. Methadone
   c. Oxycodone
   d. Morphine

8. A client with a history of opioid use disorder is prescribed naltrexone to aid in abstaining from opioid use. Which information will the nurse give the client?
   a. This drug reverses an accidental overdose.
   b. This drug blunts the effects of opioids.

c. This drug can cause euphoria.
d. This drug causes a high feeling.

9. A client reports that the current dosage of oxycodone they are taking for chronic back pain is no longer relieving the pain. The health care provider increases the dosage of oxycodone, and at a follow-up appointment the client reports that their pain is well controlled again. The nurse explains that the client is experiencing which phenomenon?
a. Adverse reaction
b. Tolerance
c. Opioid use disorder
d. Allergic reaction

10. A client recovering from a knee replacement in the postanesthesia care unit develops significant shivering. Which medication does the nurse anticipate will be ordered for this client?
a. Aspirin
b. Codeine
c. Meperidine
d. Nalbuphine

CHAPTER 15
Substance Use Disorder Treatment Drugs

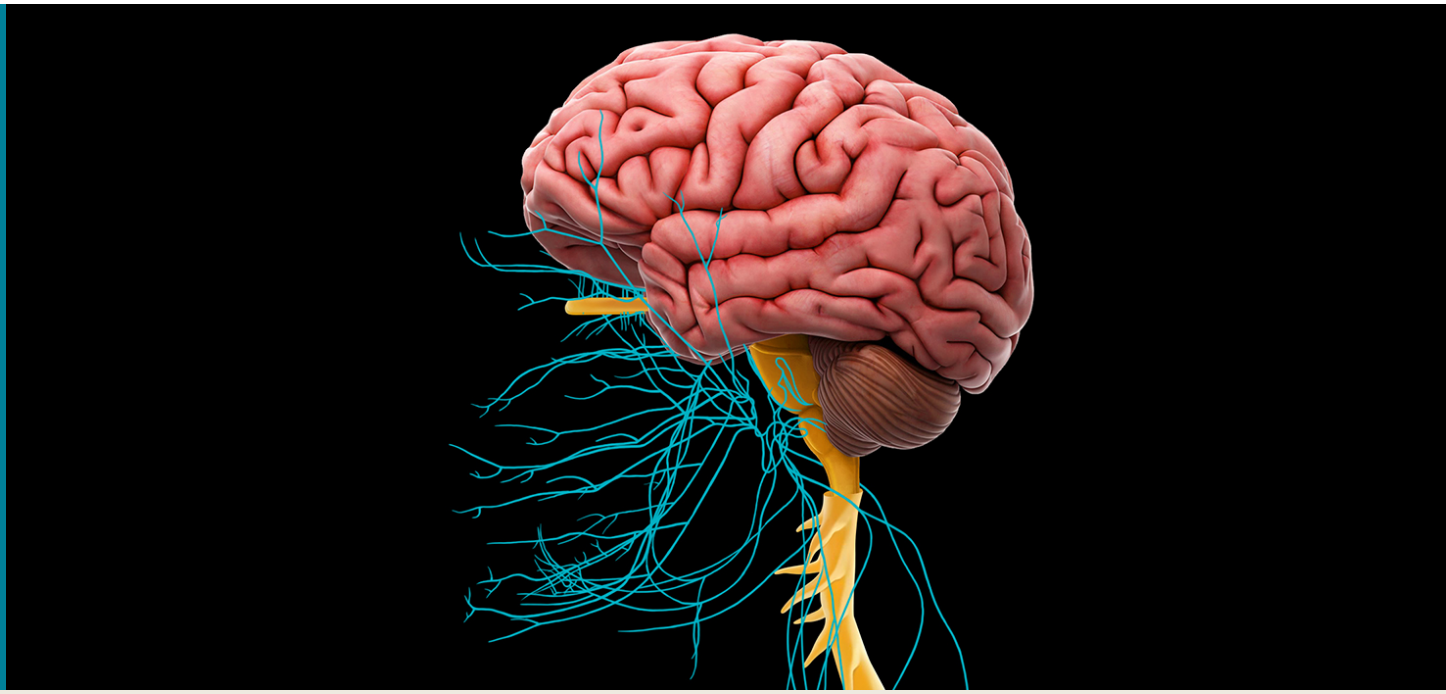


FIGURE 15.1 The nervous system, the body's control center, consists of the brain, the spinal cord, and a very complex system of nerves. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Substance use disorders are a major public health concern in the United States and affect millions of people around the world. The consequences of substance use disorders can be catastrophic for the client, their family, and society at large. As frontline health care providers, nurses play a crucial role in the prevention, identification, and treatment of clients with substance use disorders. This chapter will review the definition of substance use disorders, how to identify clients with substance use disorders, and how to manage their condition. In addition to nonpharmacologic treatment options for substance use disorders, this chapter will also review medication therapy to assist in the treatment of opioid, alcohol, and nicotine use disorders.

15.1 Introduction to Substance Use Disorders

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 15.1.1 Define intoxication, physical dependence, and psychological dependence.
- 15.1.2 Distinguish between tolerance, addiction, and withdrawal.
- 15.1.3 Describe treatment approaches for substance use disorders.

Introduction to Substance Use Disorders

The standard definition of a **substance use disorder** (SUD), from the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5), is that it involves patterns of symptoms caused by using a substance that an

individual continues taking despite its negative effects (McNeely & Adam, 2020). This chapter will primarily focus on opioid, alcohol, and nicotine use disorders, which are three of the most prevalent SUDs in the world, but this definition pertains to many other substances, including caffeine, marijuana, and stimulants (e.g., cocaine and amphetamines), to name a few.

Substance misuse disorders are quite prevalent in the United States. The National Survey on Drug Use and Health estimates that in 2021, 46.3 million people (16.5% of the population) over the age of 12 met the DSM-5 criteria for having an SUD in the past year. Of those people, 29.5 million were classified as having an alcohol use disorder and 24 million had a drug use disorder. Unfortunately, it has been estimated that 94% of individuals with SUDs felt they did not need treatment and therefore did not receive any (Substance Abuse and Mental Health Services Administration, 2023a). Several populations by age should also be considered as being at risk for SUDs that may be overlooked by health care providers. These include the nearly 1 million adults over age 65 who live with an SUD and the 2 million teenagers ages 12–17 who reported drug use (NIH, 2020; National Center for Drug Abuse Statistics, n.d.).

The consequences of SUDs should not be understated. It has been shown that SUDs are associated with over 200 types of chronic conditions or injuries, including cardiovascular disease, hepatitis, communicable diseases (e.g., human immunodeficiency virus, or HIV), and motor vehicle accidents. In addition to the physical harm that may come to the client with an SUD, it is important to also consider the additional consequences of SUDs, including decreased quality of life, strain on the client's family and friend network, legal consequences, and the risk for overdose and death (see Figure 15.2). This is why it is so critical for the nurse to be vigilant for SUDs in clients, as they may be the first health care provider to assess and identify an SUD. (See this *Nurse Journal* list (https://openstax.org/r/nursejournal) for additional resources.)

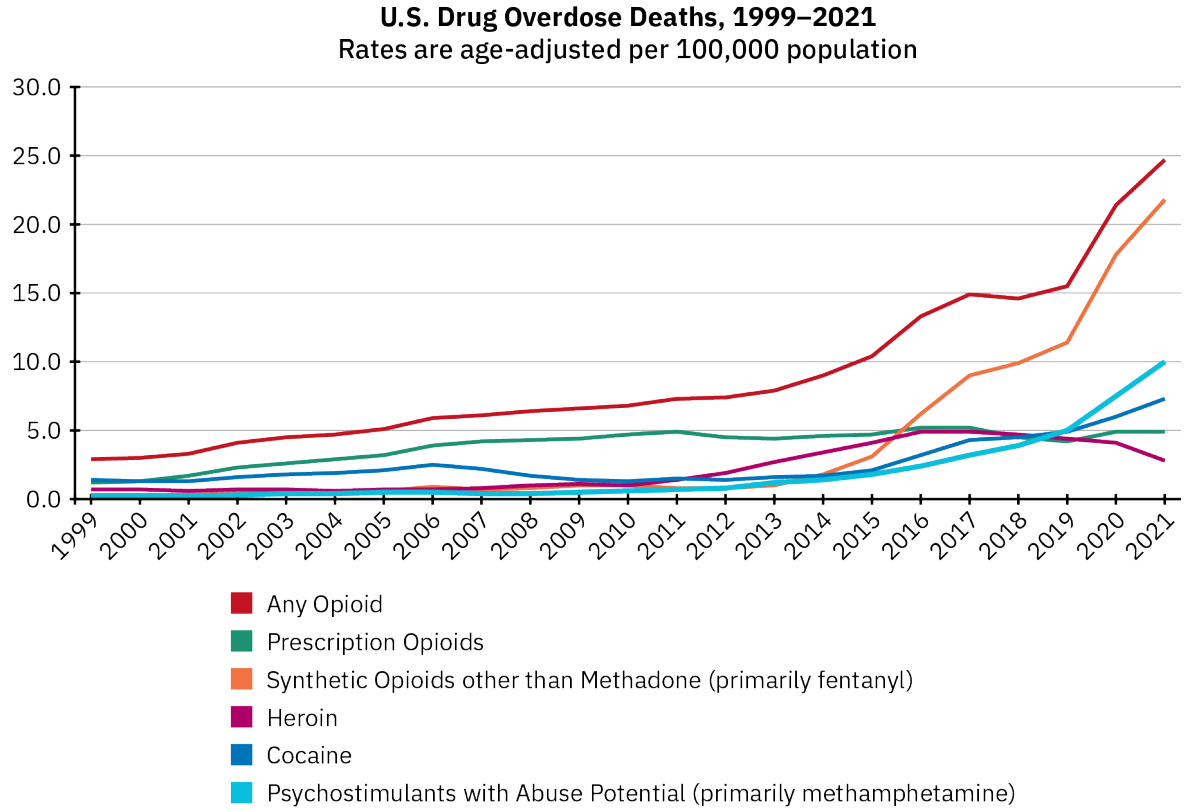


FIGURE 15.2 This graph shows overdose deaths associated with various substance abuse drugs over two decades. (data source: National Center on Health Statistics, CDC WONDER; attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Overview of Substance Use and Abuse

To understand the different aspects of SUDs and their treatments, it is important for the health care provider (HCP) to understand how these disorders begin and the physiologic changes that occur when using these substances. Key concepts for the HCP to understand are the early euphoric aspects of intoxication, leading to the physical and

psychological dependence that can make it so difficult for clients with SUDs to discontinue their habits despite the known harms.

Substances of abuse all increase the release of the neurotransmitter dopamine in the brain, which causes more pleasure and euphoria than other naturally rewarding activities. Drugs of abuse change the reward circuitry that is associated with a cycle of dependence, craving, addiction, and tolerance. This change, referred to as neuroadaptation, causes the transition from being able to control the use of the substance to chronic misuse that can be difficult to control. It is difficult to determine which individuals will be susceptible to which substances or behaviors. Ongoing research is looking into the role that one's genetics plays in the genesis of these disorders.

This section will introduce the reader to the various aspects of substance use disorders, including intoxication, physical and psychological dependence, tolerance, and withdrawal. It will include discussion about the subsequent physiological and psychological changes that lead clients to develop substance use disorders.

Substance Use Disorders and Terminology

Addiction is a historical term that has been replaced by the term "substance use disorder" but can technically refer to behaviors outside of substance use such as gambling, internet use, and shopping. The term "addiction" has a negative stigma and is no longer recommended. Substance use disorder is the term now used in the DSM-5-TR (the standard classification of mental disorders used by professionals) because tolerance and physical dependence are so often mislabeled as simply addiction. SUD is a more descriptive and accurate term that does not currently carry the same stigma. When used clinically, "addiction" should be reserved for cases of severe SUD. In short, substances may be addictive, but people are not *addicted*; they have a *substance use disorder*.

SPECIAL CONSIDERATIONS

Stigmatizing Language

Negative labels are a significant barrier to many clients with substance use disorders. Negative experiences lead clients with SUDs to avoid health care encounters, to discharge themselves from the health care environment, and to be less likely to call emergency services due to perceived ridicule and maltreatment from health care providers. This includes stigmatizing language to refer to these clients, including the term *addict*. A study has found that when health care providers are given special training to expose them to the realities of opioid use disorder, they experience a significant decrease in the number of stigmatizing views they hold. It is important for health care providers to develop a greater sense of empathy and avoid stigmatizing language to ensure that clients with SUDs feel welcome and remain willing to seek out the care they require.

(Sources: Aronowitz & Meisel, 2022; Kennedy-Hendricks et al., 2022)

Intoxication

Intoxication refers to the substance-specific physiologic effects that occur after exposure to a psychoactive substance (American Psychological Association, 2023). The effects of intoxication can vary widely depending on the mechanism of action of the specific substance the client is exposed to. For example, someone consuming alcohol will develop impaired decision-making capability, impaired memory, and general central nervous system (CNS) depression. Contrast this to the client exposed to cocaine, who may experience increased energy, hallucinations, and seizures. The intoxicating effects a client will develop are generally predictable based on the mechanism of action of the substance used. However, the effects may be unpredictable if the client is unable or unwilling to tell health care providers what they used or if the substance was contaminated with an entirely different agent (e.g., the opioid fentanyl is found in many other substances of abuse, such as cocaine).

The level of intoxication that someone will experience is extremely variable and is determined by the substance used along with the dose, frequency, and route of administration. For example, someone using the opioid heroin will have a much stronger and faster degree of intoxication after injecting the drug intravenously as opposed to ingesting it. Because of tolerance to drugs, to be discussed later, the amount of drug necessary to achieve the desired level of intoxication will often increase with time.

Physical Dependence

Physical dependence refers to the homeostatic adaptation that occurs when the body is exposed to certain

substances over a prolonged period (American Psychological Association, 2023). This adaptation means that the body becomes used to having the effect of the drug, and when that drug is removed, the body will develop a withdrawal reaction, known as abstinence syndrome. Physical dependence is not just a phenomenon that occurs with substances of abuse; it can also be seen with pharmacologic agents such as certain antihypertensives and corticosteroids. Generally, all clients with opioid, nicotine, and alcohol SUDs will develop some degree of physical dependence that is determined by the duration and amount of drug used. Health care professionals should not confuse physical drug dependence with substance use disorders, because physical dependence can occur during routine medical care and is not always indicative of an SUD. To put it another way, not all clients with physical dependence will develop an SUD, but nearly all clients with an SUD will have physical dependence to their drug of choice.

Psychological Dependence

While physical dependence deals with the physiologic reactions to the presence of substances of abuse, **psychological dependence** deals with the cognitive and behavioral aspects of SUDs that develop over time. While the body has a physical withdrawal reaction to the removal of a substance of abuse, the brain can also have a cognitive reaction. The effects of psychological dependence can include cravings to use the substance in question as well as effects that occur if the client is attempting to, or being made to, stop using the substance, including anxiety, depression, sleep disturbances, and irritability. The client may also exhibit cognitive effects, including inability to concentrate, impaired memory, and poor critical thinking skills.

Tolerance

Tolerance refers to the decrease in response to a drug after continuous use. Clients with SUDs may not develop the same degree of intoxication with the dose that they were using previously, which leads to escalations in drug dose used over time. When escalation in dose is not sufficient or practical to achieve the desired level of intoxication, the client with an SUD may substitute with stronger substances (e.g., going from using beer to hard liquors) or alternative routes of administration (e.g., going from oral use of opioids to intravenous injection). Like physical dependence, tolerance can occur with a variety of different substances during their normal course of use and should not be seen as a definitive sign of an SUD (e.g., a client with a terminal illness needing escalating doses of opioids for their chronic pain).

Withdrawal

Withdrawal refers to physiologic and psychological consequences of discontinuation or reversal of a substance that the client has been using for a sufficient period. The degree of withdrawal symptoms that are experienced is determined by the substance used, dose, duration of use, and last time of exposure to the substance in question. For example, intoxication can manifest itself in many ways based on the pharmacology of the substance used, and withdrawal will manifest, usually, as the opposite effects of the substance used. Alcohol use can cause CNS depression, whereas alcohol withdrawal can manifest as severe anxiety, hallucinations, and seizures. Withdrawal effects can vary in severity from very mild (e.g., marijuana withdrawal) to potentially life-threatening (e.g., alcohol or sedative withdrawal). Due to the potential for morbidity and mortality, the risk for withdrawal must be assessed in the client and prompt treatment administered if warranted. Withdrawal can often be a major reason that clients will either be unable to stop use of their substance of choice or relapse during periods of sobriety.

Treatment Approaches for Substance Use Disorders

Treatment of substance use disorders is complex and challenging. Unfortunately, no single approach will work for every client. It is important to not manage a substance use disorder in a vacuum but instead consider all the unique circumstances that may affect the ultimate success of treatment. These circumstances can include the nature of the client's substance use, the client's ability to secure stable housing, legal concerns, and concomitant mental and health conditions. Often, any one of these concerns can undermine a client's ability to adhere to a safe and effective treatment plan. This is why it often requires a multidisciplinary team of health care providers to devise and implement a plan of care that will work for the individual client to achieve long-term recovery. This chapter focuses on medication therapy for SUDs, but it is important to understand that the synergy of using multiple treatment modalities will increase the chances for a successful result.

One approach to treatment of substance use disorders includes behavioral therapy, such as **cognitive behavioral therapy** (CBT). This approach helps clients evaluate and change their thoughts, feelings, and behaviors related to

their substance use. It can also be helpful for dealing with concomitant mental health disorders that may contribute to the client's SUD, including depression, anxiety, bipolar disorder, and schizophrenia.

Support groups such as Alcoholics Anonymous and Narcotics Anonymous can be another avenue for approaching treatment of an SUD. These groups allow for clients to connect with other individuals with similar conditions to share their stories and receive encouragement and accountability to continue sticking with their individual plan of care.

Finally, medications can be utilized to help individuals with SUDs achieve long-term success by helping reduce cravings, minimize withdrawal effects, or otherwise make using a substance of choice less appealing than simple abstention from use. Upcoming sections will discuss the mechanism of action and rationale for use of these medications in detail.

15.2 Opioid Use Disorder Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 15.2.1 Discuss the pathophysiology of opioid use disorder disorder.
- 15.2.2 Identify clinical manifestations of opioid use disorder.
- 15.2.3 Identify the etiology and diagnostic studies related to opioid use disorder.
- 15.2.4 Identify the characteristics of drugs used to treat opioid use disorder.
- 15.2.5 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat opioid use disorder.
- 15.2.6 Describe the nursing implications of drugs used to treat opioid use disorder.
- 15.2.7 Explain the client education related to drugs used to treat opioid use disorder.

Opioid Use

Opioids are a class of drugs that activate the opioid receptors in the CNS. Opioids have been widely used for thousands of years and are derived from the opium poppy, *Papaver somniferum*. Opioids include many agents, including naturally occurring opioids such as heroin, codeine, and morphine, along with synthetically derived agents such as hydrocodone, oxycodone, and fentanyl. Opioids are well known to be powerful analgesics and antitussive agents but have also been shown to carry risk for physical dependence and opioid use disorder (OUD).

The United States is dealing with one of the biggest health crises that it has ever faced—the opioid epidemic. It is estimated that OUDs affect more than 16 million people worldwide, with over 2.1 million of those individuals residing in the United States. The biggest risk seen with use of opioids is the chance of overdose and death, which accounts for 120,000 deaths annually worldwide (Dydyk et al., 2023). This is true despite the fact that opioids are tightly regulated by the U.S. Drug Enforcement Administration (DEA). Most prescription opioids (e.g., morphine, hydrocodone) are designated as Schedule II (CII) medications, meaning they carry a substantial risk for misuse but still have an acceptable medical use. Heroin, on the other hand, is used illicitly, as it is scheduled as Schedule I (CI), meaning that it has a high abuse potential and no acceptable medical use. This means that if clients with an OUD are using CII medications without a valid prescription or any CI medications, there may be legal complications (e.g., felony arrest), which can further complicate their road to long-term recovery.

Opioid Intoxication

Opioids produce many of their desired therapeutic effects and potentially life-threatening adverse effects via the opioid receptors, including the mu, delta, and kappa receptors. Opioid intoxication is classically described as a triad of symptoms consisting of reduced consciousness, slow and/or shallow breathing, and miosis (i.e., pinpoint pupils). In addition, opioids will cause analgesia and euphoria depending on the dose and route used. Tolerance will rapidly develop to the analgesic and euphoric properties of the opioids, which leads to a rapid dose escalation to achieve the same effects that the client had been experiencing at lower doses. Clients receiving treatment for an OUD that includes abstention from opioids (e.g., stays at rehabilitation facilities) may lose tolerance over time. It is vital to educate clients about this, since clients who go on to relapse and use opioids at their previous doses may experience more opioid effects than they were intending, leading to accidental overdose and risk for death due to respiratory depression.

The presence of opioids in a client is not routinely measured in the blood but rather is detected using urine drug screens. Most traditional urine drug screens will test reliably for naturally occurring opioids such as heroin, codeine, and morphine but will potentially miss opioids that do not share the same chemical resemblance. Specific tests must be performed to detect the presence of agents such as oxycodone or fentanyl. For the clinician, it is important to keep in mind that a negative urine opioid screen does not always rule out the possibility that someone is experiencing opioid intoxication.

Opioid Withdrawal

Opioid withdrawal occurs in clients using opioids for a chronic period who have abruptly discontinued the drug, or from rapid reversal of the drug's effect with an opioid antagonist (e.g., naloxone). The onset of opioid withdrawal will vary from a few seconds to minutes after administration of a dose of a reversal agent like naloxone, or from hours to days if using an agent with a longer half-life (e.g., methadone).

The effects of opioid withdrawal may include a variety of symptoms that may be present in some clients but not others. These effects fit into several categories. Gastrointestinal effects of opioid withdrawal include severe abdominal cramping, diarrhea, nausea, and vomiting. Flu-like symptoms can occur including rhinorrhea, shivering, myalgias, and piloerection (i.e., goosebumps). Symptoms of excessive sympathetic and CNS activation include dilated pupils, tachycardia, anxiety, irritability, agitation, and tremor. Fortunately, withdrawal from opioids is rarely life-threatening, but there are rare reports of seizures occurring, so health care providers should be prepared in case these consequences arise.

Drugs Used to Treat Opioid Use Disorders

There are several drugs available to assist in the management of opioid use disorders. They include medications to reduce withdrawal symptoms and to help reduce clients' desire to begin using opioids again, such as methadone and buprenorphine. It is also important to be able to rapidly reverse the life-threatening effects of opioids in case of overdose; thus opioid antagonists, such as naloxone, are also used.

Naloxone

Naloxone is the prototypical mu opioid receptor antagonist used to rapidly reverse the life-threatening effects of opioid overdose. While naloxone is not used directly in the treatment of opioid use disorders, it is important that clients at risk for opioid overdose have quick and easy access to naloxone in case of accidental or intentional overdoses. This was made easier when naloxone was designated as an over-the-counter drug in March 2023.

Naloxone may be administered in several ways but will most commonly be given intravenously in the hospital setting and intranasally when administered by non-health care practitioners (e.g., family members, law enforcement agents). Because of the nature of opioid overdoses, clients will be too sedated to administer naloxone to themselves. Those who are most likely to be around the client should an overdose occur (e.g., family members, roommates) need to be educated on proper recognition of an opioid overdose and how to administer naloxone should the need arise. See this video for a demonstration of intranasal naloxone administration (https://openstax.org/r/demonstration).

A key limitation of naloxone is its short duration of action. While naloxone rapidly reverses the effects of opioids within seconds to minutes, it only lasts approximately 20–30 minutes, which is less than the duration of action of many opioids. It is imperative that whoever administers naloxone to a client should promptly call emergency services to provide definitive treatment to the client prior to the re-sedating effects of the opioid.

Naltrexone

Naltrexone is like naloxone in that it is a pure mu opioid receptor antagonist. The key difference between the two is that naltrexone is orally bioavailable. Because of this, naltrexone is not used as a rescue medication in case of opioid overdose but is used as a preventative agent. Once a client is abstinent from opioids for 5–7 days, they can then begin taking naltrexone daily. The purpose of this waiting period is to prevent an immediate withdrawal syndrome. Naltrexone will prevent the euphoric effects of opioids should the client relapse and begin using opioids again. As there are concerns about client compliance with taking a daily medication, naltrexone also comes as a long-acting, once-monthly injectable form to ensure compliance for this period.

Buprenorphine-Naloxone

Buprenorphine is a partial mu opioid receptor agonist that is designed to reduce the symptoms of opioid withdrawal and cravings in clients abstaining from opioid use. The inclusion of naloxone with oral preparations of buprenorphine may seem nonsensical given that naloxone has poor oral bioavailability, but this is done to discourage intravenous abuse of buprenorphine, as the naloxone would cancel out the euphoric effects of buprenorphine upon injection. The inclusion of naloxone in these oral dosages is a form of **abuse deterrence**. Buprenorphine by itself also comes in a variety of dosage forms, including long-acting injectables and transdermal patches. Buprenorphine has a high affinity for the opioid receptor and can displace other opioids that can cause opioid withdrawal to occur. Because of this, buprenorphine should be initiated once withdrawal symptoms begin to occur to reduce these symptoms to aid in opioid abstention.

Methadone

Methadone is a full mu opioid receptor agonist that has been used for many years to wean clients off opioids. Being a full agonist, methadone can help reduce or prevent opioid withdrawal symptoms and allow for a gradual tapering down of the methadone dose until the client no longer requires it. Methadone is used over other opioids because it has a long half-life of up to 59 hours. Since methadone is a full opioid agonist and carries the same risk for abuse as other opioids (e.g., morphine, heroin), clients are not given a full month's worth of methadone at a time like a typical prescription. Instead, methadone must be given in a monitored setting as a part of **direct observed therapy**. The long half-life of methadone allows for levels of the drug to build up in the client's body throughout the week. When the clinic where the client receives their methadone is closed on the weekend, they still have high enough drug levels in the body to reduce or prevent withdrawal symptoms until the clinic opens again on Monday. This is the most traditional way for methadone to be used, but in recent years, clinicians have realized the potential for methadone to be an effective agent to treat chronic pain, so it is important for health care providers to not assume that all clients using methadone have an OUD.

Table 15.1 lists common medications used to treat opioid use disorders and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Buprenorphine-naltrexone (Suboxone)	*Maintenance treatment (sublingual):* Buprenorphine 2 mg/naloxone 0.5 mg once daily with titrations up to a target dose of buprenorphine 16 mg/naloxone 4 mg once daily.
Buprenorphine (Buprenex)	*Sublingual:* 2–4 mg once daily. *Subcutaneous:* 100 mg once monthly after induction and dose stabilization.
Methadone (Dolophine)	*Induction/initial dosing:* 20–30 mg orally once daily; titrate to a dose sufficient to suppress withdrawal symptoms.
Naloxone (Narcan)	*Opioid overdose (known or suspected):* *Intravenous (IV):* 0.4–2 mg as needed. *Intranasal:* 4–8 mg as needed in one nostril every 2–3 minutes until medical assistance is available.
Naltrexone (Vivitrol)	*Oral:* 25–50 mg daily. *Intramuscular:* 380 mg every 4 weeks.

TABLE 15.1 Drug Emphasis Table: Medications Used to Treat Opioid Use Disorder (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

The primary adverse effect of opioid antagonists like naloxone and naltrexone is the risk of inducing opioid withdrawal in clients chronically taking opioids. Clients generally should be abstaining from opioids prior to initiation of naltrexone therapy and should be under medical supervision in the case of severe withdrawal reactions.

Since buprenorphine is a partial opioid receptor agonist, it can still cause symptoms of opioid intoxication including CNS and respiratory depression. This is especially true for accidental ingestions of buprenorphine by children and animals. Like other full opioid agonists, methadone carries the same risk for problematic use and risk for overdose causing life-threatening CNS and respiratory depression. Methadone can prolong the QTc interval on an electrocardiogram (ECG, EKG), and clients should be monitored if taking multiple medications that prolong the QTc

interval due to risk for the ventricular dysrhythmia torsades de pointes.

Table 15.2 is a drug prototype table for medications used to treat opioid use disorders featuring buprenorphine-naloxone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Partial opioid agonist/opioid antagonist **Mechanism of Action** Used as a partial agonist at the mu opioid receptor. Naloxone is an opioid antagonist and produces opioid withdrawal signs and symptoms in individuals physically dependent on full opioid agonists when administered parenterally	**Drug Dosage** *Maintenance treatment (sublingual):* Buprenorphine 2 mg/naloxone 0.5 mg once daily with titrations up to a target dose of buprenorphine 16 mg/naloxone 4 mg once daily.
Indications Maintenance treatment of opioid dependence **Therapeutic Effects** Reduces opioid withdrawal symptoms	**Drug Interactions** Benzodiazepines Cytochrome P450 3A4 inhibitors Cyclobenzaprine Diphenhydramine **Food Interactions** Ethanol
Adverse Effects Diaphoresis (excessive sweating) Abdominal pain Constipation Headache Pain Withdrawal syndrome Vasodilation Vomiting Hepatocellular injury	**Contraindications** Hypersensitivity Caution: Substance abuse and misuse Respiratory depression CNS depression Hepatic dysfunction

TABLE 15.2 **Drug Prototype Table: Buprenorphine-Naloxone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking a medication for OUD:

- Determine the client's last use of an opioid prior to starting naltrexone or buprenorphine-naloxone to avoid withdrawal reactions.
- Advise the client and those close to them how to recognize an opioid overdose and how to administer intranasal naloxone.
- Advise the client and those close to them to call emergency services any time that naloxone is given.
- Observe for withdrawal symptoms, including anxiety, diarrhea, piloerection, and sweating.
- Assess for changes in level of consciousness and respirations.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

SAFETY ALERT

Methadone

Methadone can have variable pharmacokinetics in clients based on their individual genetics, along with interacting medications that can affect its metabolism. Prior to adding any new medications to a client's regimen, it is imperative to check for any interactions and monitor for increased or reduced effects of methadone and

adjust its dose accordingly. Clients should be educated to disclose that they are on methadone to prescribing health care providers to ensure that these interactions are monitored. This information should include the indication for the client's methadone use and current dose. Most current dosing information should be obtained from the clinic where the client receives methadone. Methadone can also prolong the client's QTc interval as measured on an ECG and can increase the risk of fatal dysrhythmias. Use cautiously in clients with a history of congenital prolonged QT syndrome or who are taking multiple medications that prolong the QTc interval.

CLIENT TEACHING GUIDELINES

The client taking a medication for OUD should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert their health care provider about any recent opioid medication use prior to starting therapy.
- Alert other health care providers that they are taking these OUD medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should not take double doses.
- Avoid abrupt discontinuation of medications used to treat OUD to avoid withdrawal symptoms.
- Seek out care from their health care provider if they notice dark urine, light-colored stools, right upper quadrant pain, nausea, or yellow sclera.
- Seek out community services to aid in SUD treatment, including organizations such as Narcotics Anonymous.
- Increase intake of fluid to prevent constipation.

TRENDING TODAY

X-Waiver Requirement

In the United States, there is a severe lack of specially trained health care practitioners able to provide OUD treatment with agents such as methadone. There has been a push recently to increase the ability for health care practitioners to treat clients with OUD in the primary care setting with agents such as buprenorphine. Buprenorphine has a greater safety margin than methadone, so it can be prescribed with relative safety by physicians, nurse practitioners, and physician assistants. In the past, nurse practitioners and physician assistants who wanted to prescribe buprenorphine needed a DEA license in addition to specialized training to receive authorization to prescribe buprenorphine. This authorization was known as an X-waiver. As of 2023, this X-waiver requirement has been removed, opening the door to a much wider number of prescribers who can manage OUDs and increasing access for those clients with an OUD. Thus, you may see a wider adoption of buprenorphine for treatment of OUDs.

CLINICAL TIP

Assess for Most Recent Opioid Use

When initiating therapy with buprenorphine or naltrexone, it is important to assess the client's most recent opioid use. If therapy is initiated and the client has recently used an opioid, it is likely the client will experience moderate to severe withdrawal symptoms. This can be difficult due to clients commonly being hesitant to share recent drug use, so fostering an open and nonjudgmental environment will help to promote honest communication with the client.

UNFOLDING CASE STUDY

Part A

Read the following clinical scenario to answer the questions that follow. This case study will evolve throughout the chapter.

Daniel Nguyen is a 34-year-old client who presents to his health care provider's office stating that he wishes for help with his prescription opioid use.

History

Opioid use disorder: takes prescription oxycodone when he can acquire it
Cigarette smoking: smokes 1 pack per day for 7 years
Major depressive disorder
Chronic back pain—developed after a workplace injury at his construction job 5 years ago

Current Medications

Duloxetine 40 mg orally daily
Oxycodone 20 mg orally as needed for pain

Vital Signs		Physical Examination
Temperature:	98.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; no peripheral edema noted bilaterally; S1, S2 noted, rhythm regular • *Respiratory:* Clear to auscultation bilaterally • *GI:* Abdomen soft, nontender, nondistended • *GU:* Reports normal urine output • *Neurological:* Alert and oriented to person, place, and time; no motor deficits noted • *Integumentary:* No wounds noted; skin color appropriate for age
Blood pressure:	126/75 mm Hg	
Heart rate:	78 beats/min	
Respiratory rate:	16 breaths/min	
Oxygen saturation:	99% on room air	
Height:	5'8"	
Weight:	175 lb	

TABLE 15.3

1. Based on the information above, what is a priority question for the nurse to ask Daniel?
   a. "Have you ever been arrested?"
   b. "When was your last opioid use?"
   c. "Where do you get your opioids from?"
   d. "Have you lost or gained weight recently?"

2. What effects of opioid withdrawal should the nurse educate the client about that can happen if he continues taking opioids along with naltrexone?
   a. Hypotension
   b. Respiratory depression
   c. Lethargy
   d. Diarrhea

FDA BLACK BOX WARNING

Benzodiazepines and Opioids

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of these drugs for clients for whom alternative options are inadequate. Limit dosages and durations to the minimum required.

Buprenorphine

Serious, life-threatening, or fatal respiratory depression may occur with the use of buprenorphine.

15.3 Alcohol Use Disorder Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 15.3.1 Describe the pathophysiology of alcohol use disorder.
- 15.3.2 Identify clinical manifestations of alcohol use disorder.
- 15.3.3 Identify the etiology and diagnostic studies related to alcohol use disorder.
- 15.3.4 Identify the characteristics of drugs used to treat alcohol use disorder.
- 15.3.5 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat alcohol use disorder.
- 15.3.6 Describe the nursing implications of drugs used to treat alcohol use disorder.
- 15.3.7 Explain the client education related to drugs used to treat alcohol use disorder.

Alcohol Use

Alcohol, more specifically *ethanol*, is the byproduct of the fermentation of carbohydrates and is one of the most widely used psychoactive compounds in the world. While alcohol is legal to purchase and seen as a socially acceptable substance for recreational use, it is also a major contributor to significant morbidity and mortality. In the United States alone, alcohol has been causally linked to over 200 different chronic health conditions (e.g., hepatitis, diabetes, heart disease) and contributes to 18.5% of emergency department visits (Rehm et al., 2021). Annually, alcohol contributes to 95,000 deaths, making it one of the leading causes of preventable death in the United States. Despite the known harms of alcohol, it is estimated that there are 29.5 million people over age 12 in the United States with an alcohol use disorder (AUD) (Substance Abuse and Mental Health Services Administration, 2023a).

Alcohol works by increasing the actions of gamma-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the brain. When GABA activates GABA-A receptors, it leads to an influx of chloride into the neuron, hyperpolarizing it and making the generation of action potentials more difficult. When enhanced by the actions of alcohol and other sedative drugs, this leads to an overall slowing of neuronal transmission and produces the characteristic effects of alcohol intoxication (e.g., slurred speech, stumbling gait, memory impairment).

Alcohol Intoxication

Alcohol intoxication follows a predictable dose response in clients with low or no routine alcohol consumption. At low doses, alcohol lowers inhibitions and can cause a mild euphoria. At moderate doses, ethanol will cause ataxia (e.g., gait instability), slurred speech, and impaired memory. At higher doses, alcohol can cause total memory loss (i.e., blackouts), CNS depression, and risk for respiratory depression. The risk for respiratory depression and death increases significantly if consumed along with other CNS depressants (e.g., opioids, benzodiazepines). Alcohol intoxication may also lead to nausea and vomiting. If the client is sufficiently CNS depressed and vomits, there is a risk for the client to aspirate their stomach contents, leading to respiratory failure and death. Another concern with alcohol intoxication is the risk for trauma, including fatal head traumas because of falls. Certain clients may be prone to violence under the effects of alcohol, leading to altercations. Impaired decision making can lead clients to operate motor vehicles, leading to motor vehicle accidents.

The degree of alcohol intoxication can be determined objectively by measuring the blood alcohol level directly with a blood sample or indirectly, such as with a device that measures alcohol content in the expired air of the intoxicated client (i.e., a breathalyzer). The legal definition of drunkenness can vary by location but is considered in many places to be a blood alcohol level of 0.08% or 80 mg/dL.

Alcohol Withdrawal

Alcohol withdrawal occurs when the client who chronically uses alcohol has an abrupt discontinuation of the substance. Because of the chronic increase in GABA effects in the CNS, GABA receptors become **downregulated**. When alcohol is removed, the client will experience a shift toward the actions of glutamate, the major excitatory neurotransmitter in the CNS. This leads to the opposite actions of alcohol where clients may develop anxiety, restlessness, piloerection, hallucinations, and seizures. Severe alcohol withdrawal is commonly referred to as **delirium tremens**. Withdrawal from alcohol may begin as soon as a few hours after the last consumption of alcohol but may take 2–3 days to fully manifest. As compared to the minimal risk of death seen with opioid withdrawal, alcohol withdrawal can be fatal and should be managed promptly to avoid withdrawal-related delirium and seizures.

Drugs Used to Treat Alcohol Use Disorders

This section covers medications used in the treatment of alcohol use disorders, including agents to treat the potentially life-threatening withdrawal symptoms as well as agents to deter the client from further use of alcohol. Indications for when to use these medications, along with their own precautions, are also given to ensure the safe and appropriate use in clients with alcohol use disorders.

Chlordiazepoxide

Chlordiazepoxide falls into the category of drugs known as benzodiazepines. These drugs, like alcohol, work to enhance the actions of GABA to cause a general CNS depression. Benzodiazepines bind to the benzodiazepine receptor to allow GABA to bind to the receptor more readily, increasing its effects. Benzodiazepines are used for a variety of conditions, including anxiety and seizures, but in the case of AUD, they serve as a replacement for alcohol to treat and/or prevent withdrawal symptoms. Clients with significant AUD should be monitored for seizures with rescue medications, including chlordiazepoxide, available at a moment's notice. Historically, chlordiazepoxide has been used to treat AUD because of its long half-life. This long half-life means chlordiazepoxide stays in the body longer, thus preventing abrupt withdrawal symptoms from occurring. Chlordiazepoxide is still available commercially but has been replaced with newer benzodiazepines because of their more favorable pharmacokinetics. The downside of chlordiazepoxide's long half-life is that it tends to accumulate in the client's body, leading to oversedation, especially when combined with alcohol should the client relapse during treatment.

Disulfiram

Disulfiram is a drug that works by inhibiting the actions of the enzyme acetaldehyde dehydrogenase. In the liver, alcohol is first metabolized by the enzyme alcohol dehydrogenase, which converts it to acetaldehyde. Acetaldehyde is then further metabolized by acetaldehyde dehydrogenase. Acetaldehyde itself is a very irritating substance that in excess will cause facial flushing, nausea, vomiting, and headaches. Interestingly, an inherited deficiency of acetaldehyde dehydrogenase is found in 8% of people in the world overall, and in 36% of Asian people, leading to a familiar flushing reaction upon consuming alcohol (Jeon et al., 2022). Disulfiram is used to intentionally inhibit acetaldehyde dehydrogenase to cause a client to develop this uncomfortable reaction should they relapse and consume alcohol. In this way, it serves as a deterrent to alcohol consumption rather than a means to replace alcohol to manage withdrawal symptoms. As disulfiram is only available as an oral tablet, client compliance with disulfiram therapy may be poor, as they may opt to just not take the medication. To initiate disulfiram therapy, clients should abstain from alcohol for at least 12 hours since their last drink to avoid a flushing reaction. Clients should also be educated that disulfiram reactions can occur up to 2 weeks after drug discontinuation and that they should avoid alcohol consumption during this time to avoid flushing reactions.

Haloperidol

Haloperidol is in the category of medications known as first-generation antipsychotics and is traditionally used to treat the symptoms of schizophrenia. It works by blocking dopamine-2 (D2) receptors that cause hallucinations and agitation. Haloperidol is sedating, and this is thought to help manage the symptoms of alcohol withdrawal in conjunction with benzodiazepine therapy.

Lorazepam

Like chlordiazepoxide, lorazepam is a benzodiazepine used to treat anxiety and seizures and to control the symptoms of alcohol withdrawal. Replacement of alcohol with lorazepam helps prevent and/or minimize withdrawal symptoms, and it is the drug of choice to treat alcohol withdrawal-induced seizures. In the hospital setting,

validated scales such as the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) use a symptoms-based approach to manage the symptoms of alcohol withdrawal as they occur and allow for a more customized approach based on which withdrawal symptoms manifest in the client and their severity. These scores are recorded by the client's nurse initially every 4 hours and can be checked less frequently as the client's withdrawal symptoms improve. This allows providers to determine the most appropriate dose of lorazepam needed to manage the client's current withdrawal symptoms.

Table 15.4 lists common medications used to treat alcohol use disorders and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Chlordiazepoxide (Librium)	*Management of alcohol withdrawal symptoms:* Initial dose 50–100 mg orally followed by repeated doses as needed up to 300 mg/day.
Disulfiram (Antabuse)	125–500 mg orally daily.
Haloperidol (Haldol)	*Management of alcohol withdrawal symptoms:* *Oral:* 2–10 mg every 6 hours as needed; maximum dose: 20 mg/day. *Intramuscular:* 2–10 mg every 6 hours as needed; maximum dose: 20 mg/day.
Lorazepam (Ativan)	*Management of alcohol withdrawal symptoms:* *IV:* 1–4 mg every 4–6 hours as needed.

TABLE 15.4 Drug Emphasis Table: Medications Used to Treat Alcohol Use Disorder (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Like alcohol, the main adverse effects of chlordiazepoxide and lorazepam are sedation and memory impairment. Clients should be educated to avoid operating heavy machinery while using these medications. Use of benzodiazepines is contraindicated in pregnancy.

The main adverse reactions seen with disulfiram occur when clients drink alcohol while taking the medication and include nausea, vomiting, skin flushing, and feeling hot.

Haloperidol can lower the seizure threshold, which increases the risk of the client developing alcohol withdrawal-related seizures. Because of this, haloperidol is not routinely recommended for this indication. Other side effects associated with haloperidol include sedation and the rare risk of sudden cardiac death (Dar et al., 2020).

Table 15.5 is a drug prototype table for medications used to treat alcohol use disorders featuring disulfiram. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Irreversible acetaldehyde dehydrogenase inhibitor **Mechanism of Action** Inhibits the enzyme acetaldehyde dehydrogenase, producing a sensitivity to alcohol that results in a highly unpleasant reaction when the client under treatment ingests even small amounts of alcohol	**Drug Dosage** 125–500 mg orally daily.
Indications Aiding in alcohol cessation (maintaining alcohol abstinence) **Therapeutic Effects** Helps support alcohol cessation by making its consumption unpleasant	**Drug Interactions** Metronidazole Isoniazid Phenytoin Tinidazole Warfarin **Food Interactions** Ethanol Kombucha
Adverse Effects Hepatitis/hepatotoxicity Drowsiness Headache Peripheral neuropathy Allergic dermatitis Metallic taste Heart failure	**Contraindications** Recent use of alcohol or metronidazole Hypersensitivity Psychoses Severe myocardial disease Severe pulmonary disease Chronic renal impairment Caution: Diabetes Rubber contact dermatitis Hepatic impairment Seizures

TABLE 15.5 **Drug Prototype Table: Disulfiram** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking a medication for AUD:

- Advise the client to avoid consuming alcohol with any of these medications due to the risk for adverse reactions. Even small amounts of alcohol may cause a reaction.
- Monitor for seizure activity in clients receiving haloperidol for treatment of alcohol withdrawal.
- Monitor the client's liver function tests to assess for liver toxicity.
- Use the CIWA-Ar scale to assess alcohol withdrawal symptoms to determine appropriate dosing of lorazepam.
- Advise clients to not take multiple CNS depressants (e.g., alcohol, lorazepam, and chlordiazepoxide) at the same time to avoid excessive CNS and respiratory depression.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

! SAFETY ALERT

Benzodiazepines

Benzodiazepines such as lorazepam and chlordiazepoxide should generally not be used at the same time as other CNS depressants such as alcohol, muscle relaxants, or opioids, as these effects can synergize and increase the risk of severe CNS and respiratory depression. Concomitant use of any combination of these agents should be done under the direction of a skilled clinician.

CLIENT TEACHING GUIDELINES

The client using a medication to treat AUD should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Alert other health care providers that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should not take double doses.
- Avoid consuming these medications with alcohol.
- Avoid taking other medications that cause sedation.
- Avoid consuming nontraditional sources of alcohol, including mouthwashes, cough syrups, hand sanitizers, and any other product that contains alcohol.
- Seek out community organizations such as Alcoholics Anonymous to aid in the treatment of AUD.

CLINICAL TIP

Assess for Cognitive Impairment in Older Adults

Older adult clients receiving benzodiazepines such as chlordiazepoxide and lorazepam to treat an AUD should be assessed for cognitive impairment (e.g., memory impairment, executive dysfunction), because this client population is more sensitive to the sedative effects of the medications.

FDA BLACK BOX WARNING

Benzodiazepines

The use of benzodiazepines, including **chlordiazepoxide** and **lorazepam**, exposes users to risks of abuse, misuse, and addiction (dependence), which can lead to overdose or death.

Disulfiram should never be administered to a client when they are in a state of alcohol intoxication or without their full knowledge. The provider should instruct relatives accordingly.

15.4 Nicotine Use Disorder Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 15.4.1 Describe the pathophysiology of nicotine use disorder.
- 15.4.2 Identify clinical manifestations of nicotine use disorder.
- 15.4.3 Identify the etiology and diagnostic studies related to nicotine use disorder.
- 15.4.4 Identify the characteristics of drugs used to treat nicotine use disorder.
- 15.4.5 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat nicotine use disorder.
- 15.4.6 Describe the nursing implications of drugs used to treat nicotine use disorder.
- 15.4.7 Explain the client education related to drugs used to treat nicotine use disorder.

Nicotine Use

Nicotine is derived from the tobacco plant and has been in use for thousands of years. It is a highly addictive substance that facilitates great harm in clients who have nicotine use disorder (NUD). It is estimated that in the United States, more than 480,000 deaths are attributable to tobacco products, making it the number-one cause of preventable death in the country. While tobacco use has declined over the past several decades, it is estimated that 50.6 million people in the United States currently use tobacco products (Cornelius et al., 2020). Tobacco products come in a variety of forms, including cigarettes, cigars, chewing tobacco, and vaping devices. Nicotine itself is not

necessarily that toxic in doses used in clients with NUDs, but it is often the other components found in tobacco products (e.g., formaldehyde, lead, arsenic, benzene, carbon monoxide) that the client is exposed to that lead to a variety of chronic health conditions such as cancer, respiratory disease, and cardiovascular disease.

Nicotine works as an agonist at the nicotinic acetylcholine receptor. At high doses, nicotine can stimulate dopamine release in the reward center of the brain, leading to many of the craving symptoms clients experience when attempting to treat NUD. Nicotine also can increase alertness and provide a feeling of pleasure and relaxation. Additionally, nicotine is an appetite suppressant, leading to some weight loss. Nicotine at extremely high doses (e.g., a child ingests unsecured vaping solution or swallows chewing tobacco) can cause significantly more toxic effects, including risks for dysrhythmia, seizures, and respiratory failure, and should be treated as a medical emergency. A relatively recent development in the consumption of nicotine is the development of vaping devices that can provide nicotine without the need to inhale hot gases as one would with a traditional cigarette. Some clients may harbor the idea that vaping devices do not contain nicotine or are safer than other sources of nicotine, but the health care provider should educate clients that these devices can be just as addictive as smoking. Vaping devices provide an additional challenge as this market is not as tightly regulated as other forms of tobacco, so there are no child-resistant safety features required on these products. Poor regulation also means that vaping solutions have been found to contain contaminants such as heavy metals, which may cause their own health risks. Vaping device malfunction has also led to device explosion, causing trauma to the hands and face.

Nicotine Withdrawal

After chronic use of tobacco-containing products, the body will develop a degree of tolerance and physical dependence. Discontinuation results in nicotine withdrawal that makes treatment of a NUD extremely difficult with exceedingly high relapse rates. Reactions that occur during nicotine withdrawal include anxiety, difficulty concentrating, irritable mood, and severe cravings for nicotine. The onset of nicotine withdrawal depends on how much nicotine is built up in the client's body. It usually begins within 24 hours after discontinuation of nicotine-containing products and can last from days to weeks, making relapse rates quite high without the assistance of behavioral and pharmacologic intervention. Like opioid withdrawal, nicotine withdrawal is not expected to be fatal.

Drugs Used to Treat Nicotine Use Disorders

This section covers medications used to treat nicotine use disorders. These include medications that are able to replace the nicotine that a client was previously using along with agents that help reduce the withdrawal symptoms and feelings of craving that may lead to clients relapsing and using nicotine again.

Bupropion

Bupropion is traditionally used for the treatment of anxiety and depression, but it has also been found to help aid in the treatment of NUDs. Bupropion's mechanism of action is that it inhibits the reuptake of dopamine and norepinephrine. How bupropion works to treat NUDs is unclear currently, but it is theorized that bupropion reduces craving symptoms for nicotine by increasing dopamine activity in the reward center of the brain. Bupropion can be advantageous in those individuals with concomitant NUD and depression and/or anxiety. Since bupropion does not have any actions at the nicotinic receptor, it is safe if clients relapse and begin using nicotine-containing products while taking bupropion.

Nicotine (NicoDerm/Nicorette)

Nicotine replacement therapy (NRT) is designed to replace the nicotine products that a client is currently using with products only containing nicotine. This helps reduce withdrawal symptoms and aids in the successful transition to using no nicotine. These come in a variety of dosage forms, including gums, patches, nasal sprays, lozenges, and inhalers. The appropriate dose to start a client on is highly dependent on the amount of nicotine being used by the client prior to quitting, due to physical and psychological dependence developed at higher doses.

While clients have successfully treated NUDs with vaping devices, it is important to recommend using FDA-approved products first, as these are highly regulated products and are held to a high standard for manufacturing and packaging. This is different from unregulated nicotine-containing vaping solutions, which have no FDA oversight and have been found to contain unadvertised products such as the heavy metals chromium, nickel, and lead. It is also important for clients who relapse and start using nicotine-containing products again to discontinue their NRT. This prevents the client from being exposed to even higher doses of nicotine than they were originally using and reduces

the risk for adverse effects.

Varenicline

Varenicline is a partial nicotine receptor agonist that has a greater affinity for the receptor than nicotine itself. Just as buprenorphine partially activates opioid receptors to reduce withdrawal symptoms and prevent other opioids from working as well, varenicline possesses the same actions for nicotine. Nicotine is safe to use if the client relapses and begins using nicotine-containing products again. In fact, it is recommended that varenicline be initiated 1 week prior to the chosen quit date to ease the transition into nicotine abstinence.

Table 15.6 lists common medications used to treat nicotine use disorder and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Bupropion (Zyban)	150 mg orally twice daily. Maximum dose: 300 mg/day.
Nicotine (NicoDerm/Nicorette)	*Gum:* 2–4 mg chewed every 1–2 hours; maximum 24 pieces/day. *Transdermal:* One 7–21 mg patch every 24 hours applied topically daily.
Varenicline (Chantix)	*Days 1–3:* 0.5 mg orally once daily. *Days 4–7:* 0.5 mg orally twice daily. *Days 8–84:* 1 mg orally twice daily.

TABLE 15.6 Drug Emphasis Table: Medications Used to Treat Nicotine Use Disorder (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Bupropion should be used cautiously in clients with a history of seizures, as this can be worsened in the presence of bupropion. Bupropion, like other antidepressant medications, can increase risk for suicidal ideation, so it is important to educate the client to monitor for depressed mood and suicidal thoughts. Bupropion can also induce manic symptoms if the client has bipolar disorder. Bupropion should be avoided if the client is taking any other drugs that increase norepinephrine actions, such as selective norepinephrine reuptake inhibitors (SNRIs) (e.g., duloxetine, venlafaxine).

Side effects of nicotine replacement products generally occur when using doses exceeding what the client was using in their previous choice of nicotine-containing product. Common adverse effects include headache, oral irritation, dyspepsia, and cough.

Common adverse effects seen with varenicline include nausea, vomiting, and abnormal dreams. Varenicline should be used cautiously in clients with a history of depression and suicidal ideation or suicide attempts, as it has been shown to increase these symptoms in some clients.

Table 15.7 is a drug prototype table for the medications used to treat nicotine use disorder featuring bupropion. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Norepinephrine/dopamine reuptake inhibitor (NDRI) **Mechanism of Action** Blocks the reuptake of norepinephrine and dopamine in the CNS	**Drug Dosage** 150 mg orally twice daily. Maximum dose: 300 mg/day.
Indications Smoking cessation **Therapeutic Effects** Lessens cravings during nicotine cessation	**Drug Interactions** Clopidogrel Carbamazepine Phenytoin Haloperidol Monoamine oxidase inhibitors Levodopa Digoxin **Food Interactions** Ethanol
Adverse Effects Anxiety Insomnia Tinnitus Tachycardia Diaphoresis Weight loss Constipation Nausea Vomiting Xerostomia (dry mouth) Agitation Tremor Blurred vision	**Contraindications** Hypersensitivity Increased seizure risk CNS infection CNS tumor Head injury Anorexia or bulimia nervosa (prior or current) Caution: Cognitive impairment Hypertension Weight loss Cardiovascular disease Hepatic impairment Renal impairment

TABLE 15.7 **Drug Prototype Table: Bupropion** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking a medication for NUD:

- Monitor for all sources of nicotine exposure other than just cigarettes, such as chewing tobacco and vaping devices.
- Screen for history of seizures in clients receiving bupropion.
- Advise discontinuing NRT if the client decided to begin using nicotine-containing products again.
- Screen for use of nicotine vaping solutions when asking about nicotine use.
- Monitor for signs and symptoms of worsening depression/suicidal thoughts while clients are taking bupropion or varenicline.
- Provide positive reinforcement to clients attempting to stop their nicotine use to help encourage compliance with their NUD therapy.
- Monitor sleep patterns.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

SAFETY ALERT

Nicotine Replacement Therapy

Clients should discontinue all nicotine replacement therapies if tobacco product consumption resumes. If not, excessive nicotine toxicity (e.g., tachycardia, dizziness) may occur. Nicotine-containing products should also be secured in a manner to avoid accidental pediatric exposures, as nicotine exposures in young children can cause severe toxicity, including the risk for respiratory failure and death. Avoid nicotine sprays in clients with a history of asthma, as this can lead to asthma exacerbations.

CLIENT TEACHING GUIDELINES

The client taking a medication to treat nicotine use disorder should:

- Alert their health care provider about any signs of allergic reactions, including throat swelling, severe itching, rash, or chest tightness.
- Notify their health care provider if palpitations, chest pain, anxiety, insomnia, and/or unintended weight loss occurs.
- Inform other health care providers that they are taking these medications, including the dose and frequency.
- Take the drug with food if it causes an upset stomach.
- Take a missed dose as soon as they remember; however, they should not take double doses.
- Avoid using nicotine-containing products while using nicotine replacement therapy.
- Apply nicotine patches to clean, dry areas of skin.
- Remove nicotine patches prior to undergoing MRI procedures and resume after the procedure is complete.
- Alert their health care provider if they feel any worsening depression or suicidal thoughts.
- Increase their fluid intake to avoid constipation.
- Have sugar-free hard candy or gum on hand to alleviate dry mouth.
- Reach out to support groups to receive additional encouragement and motivation to remain compliant with NUD therapy.

CLINICAL TIP

Assess for Changes in Dreaming in Clients Receiving Varenicline

Clients receiving varenicline are known to develop particularly vivid dreams, which can include nightmares. Clients should be educated about this possibility and report back about any dream changes, as this may require a change in therapy.

UNFOLDING CASE STUDY

Part B

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up to Case Study Part A.

Six months after the last encounter, Daniel Nguyen, a 34-year-old client, presents to the primary care provider and reports that he has been doing well after starting therapy with buprenorphine-naloxone and reports no other opioid use. He states that withdrawal symptoms are minimal and manageable. He states that he now wishes for help with his cigarette-smoking habit.

History

Opioid use disorder: being treated with buprenorphine-naloxone

Cigarette smoking: smokes one pack per day for 7 years
Major depressive disorder

Current Medications
Buprenorphine-naloxone: 16 mg/4 mg orally daily
Duloxetine: 40 mg orally daily

Vital Signs		Physical Examination
Temperature:	98.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; no peripheral edema noted bilaterally; S1, S2 noted, rhythm regular • *Respiratory:* Clear to auscultation bilaterally • *GI:* Abdomen soft, nontender, nondistended • *GU:* Reports adequate urine output • *Neurological:* Alert and oriented to person, place, and time; no motor deficits noted • *Integumentary:* No wounds noted; skin color appropriate for age
Blood pressure:	123/78 mm Hg	
Heart rate:	74 beats/min	
Respiratory rate:	16 breaths/min	
Oxygen saturation:	99% on room air	
Height:	5'8"	
Weight:	175 lb	

TABLE 15.8

3. Based on the information above, the nurse anticipates that the prescriber will most likely choose which medication for the client?
   a. Bupropion
   b. Lorazepam
   c. Naltrexone
   d. Methadone

4. The provider prescribes varenicline for the client. When should the client discontinue use of tobacco-containing products?
   a. Immediately
   b. 1 week after starting varenicline
   c. 2 weeks before starting varenicline
   d. The same time as starting varenicline

FDA BLACK BOX WARNING

Bupropion

Antidepressants, including bupropion, increase the risk of suicidal thoughts and behavior in children, adolescents, and young adults up to and including 24 years of age in short-term trials. These trials did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in subjects between the ages of 25 and 64 years; there was a reduction in risk with antidepressant use in subjects ages 65 and older.

Chapter Summary

This chapter focused on defining the various aspects of substance use disorders and ways to manage three of the most common substance use disorders in the world today. Substance use and abuse were described in terms of the short-term effects of intoxication as well as more long-term effects such as physical dependence, tolerance, and withdrawal. Emphasis was placed on how the presence of things like tolerance and physical dependence does not always mean a client has a substance use disorder.

Drug classifications covered in this chapter focused on medications to treat opioid, alcohol, and nicotine use disorders. Medications used to treat opioid use disorders included agents to minimize withdrawal effects or to prevent opioid effects should a client relapse. Naloxone, the major opioid reversal agent, was also discussed, along with how important it is for clients to have ready access to this in case of overdose. Medications for alcohol use disorders included agents to minimize the withdrawal effects of alcohol. Also addressed was how alcohol withdrawal can be potentially fatal and should be treated as a medical emergency. Agents to aid success in smoking cessation were covered, including bupropion, which blunts cravings by affecting the reward center in the brain, and nicotine replacement therapies such as gums, patches, and inhalers.

Key Terms

abuse deterrence a drug designed to reduce the ability to abuse a substance

addiction uncontrolled use of a substance or behavior despite known harms

cognitive behavioral therapy (CBT) talk therapy designed to evaluate and change thoughts, feelings, and behaviors

delirium tremens a psychotic state that occurs during alcohol withdrawal, causing tremors, hallucinations, anxiety, and confusion

direct observed therapy treatment in which clients receive medication directly from health care providers who observe them taking it

downregulated when a response to a stimulus is reduced or suppressed

intoxication the substance-specific physiologic effects that occur after exposure to a psychoactive substance

physical dependence the homeostatic adaptation that occurs when the body is exposed to substances over a prolonged period

psychological dependence the cognitive and behavioral adaptations that occur when the body is exposed to substances chronically

substance use disorder (SUD) patterns of symptoms caused by using a substance that an individual continues taking despite negative effects

tolerance the decrease in response to a drug after continuous use

withdrawal physiologic and psychological consequences of discontinuation or reversal of a substance

Review Questions

1. A nurse is evaluating a client in the emergency department, who states that they take oxycodone chronically for cancer-related pain but forgot their medication at home while on vacation. The client is experiencing severe pain, diarrhea, piloerection, sweating, and malaise. Which of the following phenomena should the nurse tell the client they are experiencing?

a. Substance abuse
b. Tolerance
c. Withdrawal
d. Psychological dependence

2. A nurse is talking with a client at a primary care office, and the client states that they normally smoke a half pack of cigarettes per day but have recently stopped smoking abruptly. The client states they are physically fine, but they frequently find themselves thinking about smoking again and experiencing intense cravings to smoke another cigarette. Which of the following phenomena should the nurse tell the client they are experiencing?

a. Intoxication
b. Tolerance
c. Physical dependence

d. Psychological dependence

3. What is the primary purpose of the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) assessment instrument?
   a. Estimate the client's alcohol consumption
   b. Manage withdrawal symptoms
   c. Assess for system disorders related to alcohol intake
   d. Plan outpatient behavioral therapy

4. A client is brought to the emergency department via emergency services after being found in their car unresponsive to any stimuli. The nurse evaluating the client notices that they have slow, shallow breathing, are unresponsive to painful stimuli, and have pinpoint pupils. Which medication does the nurse anticipate the provider will prescribe for this client?
   a. Naloxone
   b. Chlordiazepoxide
   c. Methadone
   d. Disulfiram

5. A nurse is evaluating a client for treatment of their opioid use disorder. They have a history of intravenous use of agents such as oxycodone and heroin. Which medication is the prescriber most likely to order to deter intravenous abuse of the medication?
   a. Methadone
   b. Lorazepam
   c. Buprenorphine-naloxone
   d. Chlordiazepoxide

6. A nurse is educating a client with an opioid use disorder and their parent about how to recognize the signs and symptoms of opioid overdose and when to administer naloxone. Which of the following statements should the nurse make?
   a. "After giving naloxone, call emergency services immediately."
   b. "Naloxone will last 2–3 hours."
   c. "Naloxone has no adverse effects."
   d. "Naloxone may induce seizures."

7. A nurse is collaborating with a client with a known alcohol use disorder who has recently been prescribed disulfiram. Which clinical effect should the nurse educate the client about if they decide to consume alcohol?
   a. CNS depression
   b. Flushing
   c. Withdrawal
   d. Seizures

8. A client is being admitted to the hospital for pancreatitis, and the nurse managing the client learns that the client has a previously undisclosed alcohol use disorder and has been without any alcohol for the past 2 days. Which of the following withdrawal effects would the nurse expect this client to develop?
   a. Respiratory depression
   b. CNS depression
   c. Facial flushing
   d. Seizures

9. A client is starting nicotine replacement therapy (NRT) for their nicotine use disorder. The nurse educating the client about the medication should make which of the following points?
   a. "If a child consumes any type of NRT, it should not cause any problems."
   b. "NRT can make you sleepy, so no driving a car while using it."

c. "You should stop the NRT if you begin using tobacco again."
d. "NRT therapy will prevent tobacco products from working as well if you relapse."

10. A client is being evaluated for therapy for their nicotine use disorder. The nurse notes in their history that the client has been diagnosed with a major depressive disorder but is not currently receiving any treatment for that condition. Which of the medications used for smoking cessation would the nurse anticipate the prescribing provider will initiate to both treat the client's depression and help with smoking cessation?

a. Bupropion
b. Varenicline
c. Naltrexone
d. Chlordiazepoxide

CHAPTER 16
Introduction to the Cardiovascular System

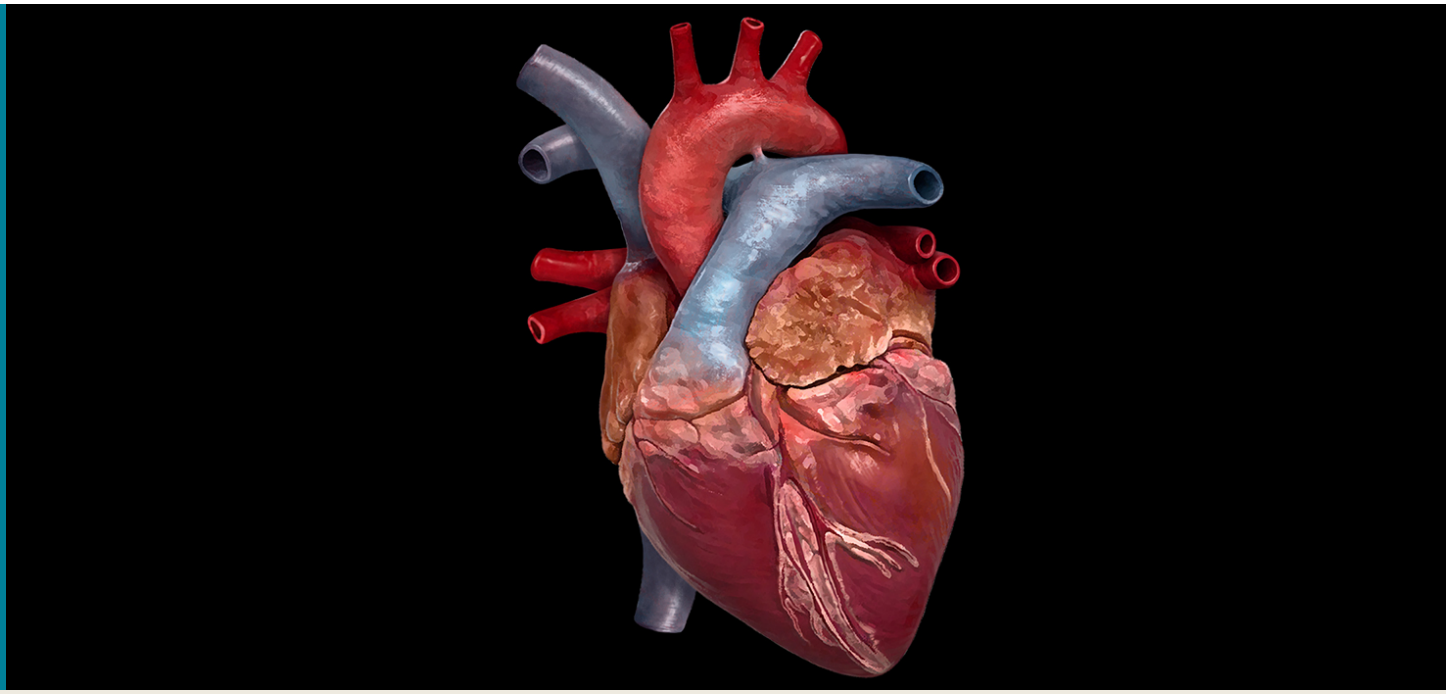


FIGURE 16.1 The heart is the primary organ of the cardiovascular system, controlling circulation and blood flow for the entire body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Cardiovascular diseases are a group of conditions related to the heart and vasculature. It includes coronary heart disease, myocardial infarction, stroke, heart failure, dysrhythmias, valvular heart disease, and others (World Health Organization, 2021). Approximately 127 million people in the United States have cardiovascular disease (Tsao et al., 2023). In 2022, the Centers for Disease Control and Prevention (CDC) reported that 1 in every 5 deaths in the United States is due to heart disease, and the estimated cost of heart disease is $239.9 billion per year (CDC, 2022).

Nurses are integral to the treatment of clients with cardiovascular disease and have many roles, including cardiovascular recovery and rehabilitation (Zhang et al., 2021). The heart is at the center of the cardiovascular system, which is a complex organ system in the human body. The heart receives deoxygenated blood from venous circulation, delivers deoxygenated blood to the lungs for gas exchange, and pumps newly oxygenated blood to the tissues for use. The reception and pumping of blood is conducted via a coordinated cardiac cycle and is regulated by an electrical conduction system. This chapter will serve as an introduction to the heart and cardiovascular system and will lay the foundation for subsequent chapters focused on the pharmacology of cardiovascular-active drugs.

16.1 Introduction to the Heart, Circulation, and Blood Flow

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 16.1.1 Describe the anatomy of the heart.
- 16.1.2 Discuss the function of the heart.
- 16.1.3 Explain circulation and blood flow within the body.
- 16.1.4 Differentiate between systemic arterial pressure and venous pressure.

Anatomy of the Heart

The heart is a fist-sized organ positioned in the central thoracic cavity, with the bulk of the heart to the left of the sternum. The heart is surrounded by a fibrous, layered sac called the pericardium. The pericardium protects the heart and provides a low-friction environment for the heart to pump in. The pericardium has two layers: the outer fibrous layer and the inner serous layer. The serous layer is made up of the parietal pericardium (which faces the fibrous layer of the pericardium) and the visceral pericardium (which lines the external heart wall). Between the parietal and visceral pericardium, there is fluid that decreases friction as the heart pumps.

The heart walls are composed of three layers: endocardium (inner layer), myocardium (middle layer), and epicardium (outer layer). The epicardium is identical to, and another term for, the visceral pericardium. The myocardium is the heart muscle that contracts to pump blood throughout the circulatory system. The cells of the myocardium are called cardiac myocytes, which are cardiac muscle cells. The endocardium is the layer that lines the inner chambers and structures of the heart, including the valves.

Figure 16.2 depicts the structure of the heart. The heart is comprised of four chambers. The two upper chambers are called the right and left **atria** (singular: atrium), which are positioned above the right and left **ventricles**, respectively.

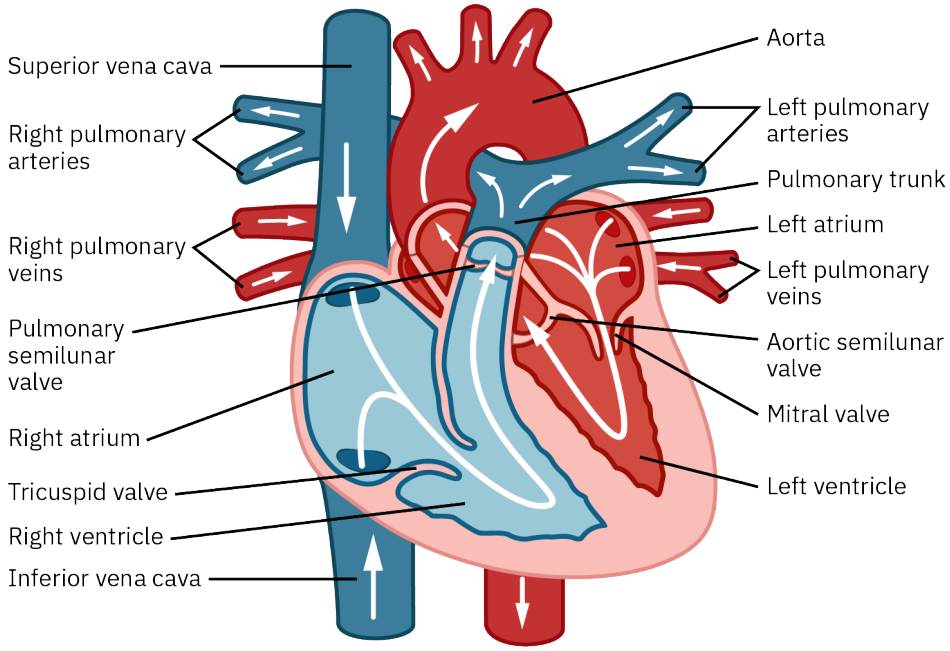


FIGURE 16.2 The human heart is structured to pump oxygenated blood to the body for use by the tissues. (credit: modification of work from *Anatomy and Physiology 2e.* attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Within the heart, valves direct blood flow and prevent the backflow of blood into the heart. These valves open and close based on pressure gradients at coordinated times within the cardiac cycle. Atrioventricular valves are positioned between the atria and ventricles. the tricuspid valve separates the right atrium and ventricle, and the mitral valve separates the left atrium and ventricle. There are also two valves positioned between the ventricles and the blood vessels they pump into. The aortic valve is positioned between the left ventricle and the aorta, and the pulmonary valve (also known as the pulmonic valve) is situated between the left ventricle and the pulmonary artery. These valves are referred to as semilunar valves because their leaflets resemble crescent moons.

The right side of the heart receives deoxygenated blood via the inferior and superior venae cavae (plural term). These are large veins that bring blood from the body and empty into the right atrium. The inferior vena cava (singular term) returns blood from the lower portions of the body, and the superior vena cava returns blood from the upper parts of the body. The heart delivers blood to and receives blood from the lungs via **pulmonary arteries** and **pulmonary veins**. The pulmonary veins carry oxygenated blood from the lungs back to the left atrium of the heart.

Although the heart pumps oxygenated blood to all tissues, the cardiac tissue also needs a supply of oxygenated blood. This is accomplished via coronary arteries that branch off of the aorta, which fill with blood during **systole** (when the heart pumps). Atherosclerotic plaques can form over time in the coronary arteries. This can eventually block blood flow to the heart, leading to ischemia (oxygen deprivation) and tissue death. This is known as a myocardial infarction, or heart attack (see Lipid-Lowering Drugs).

LINK TO LEARNING

Chambers of the Heart

Access multimedia content (https://openstax.org/books/pharmacology/pages/16-1-introduction-to-the-heart-circulation-and-blood-flow)
The National Heart, Lung, and Blood Institute provides this video showcasing a three-dimensional image of the chambers of the heart.

Function of the Heart

The main function of the heart is to pump oxygenated blood to the body for use by the tissues. To accomplish this, the heart receives deoxygenated blood from the venous vasculature and pumps the deoxygenated blood to the lungs, where gas exchange occurs. Gas exchange consists of carbon dioxide leaving the blood via exhalation from the lungs and oxygen moving from the lungs into the bloodstream. Oxygenated blood then returns to the heart and is pumped to the body for use by all the tissues. More information on the cardiac cycle is provided in the next section.

Blood is pumped via the ventricles. The right ventricle pumps against a relatively low pressure in the pulmonary system, whereas the left ventricle must pump against systemic arterial pressure to deliver oxygen. Because of this, the left ventricle is more muscular and powerful than the right ventricle.

Circulation and Blood Flow

Blood circulates from the heart to every tissue of the body. This occurs through a network of **arteries**, **capillaries**, and **veins**. Generally, arteries carry oxygenated blood away from the heart and to the tissues (Arteries = Away). Arteries are thicker-walled blood vessels and give rise to systemic arterial pressure (described in the following section). Arteries branch into arterioles (small arteries), which subdivide into even smaller branches called capillaries. Capillaries are tiny, thin-walled blood vessels that facilitate the exchange of nutrients and oxygen between blood and tissues. Venules (small veins) then collect deoxygenated blood from capillaries, channeling it into larger vessels known as veins, which return deoxygenated blood to the heart.

As mentioned previously, there is a separate circuit by which deoxygenated blood is delivered to and from the lungs for oxygenation (see Figure 16.3). This demonstrates an exception to the previously described system for arteries and veins. In the pulmonary circuit, deoxygenated blood is pumped from the right ventricle into the pulmonary artery (in systemic circulation, arteries carry only oxygenated blood). Once the deoxygenated blood is delivered to the lungs, gas exchange occurs. Carbon dioxide leaves the blood and is exhaled, and oxygen enters the blood. Once oxygenated, the blood returns to the heart via the pulmonary veins and is then pumped to the rest of the body for use.

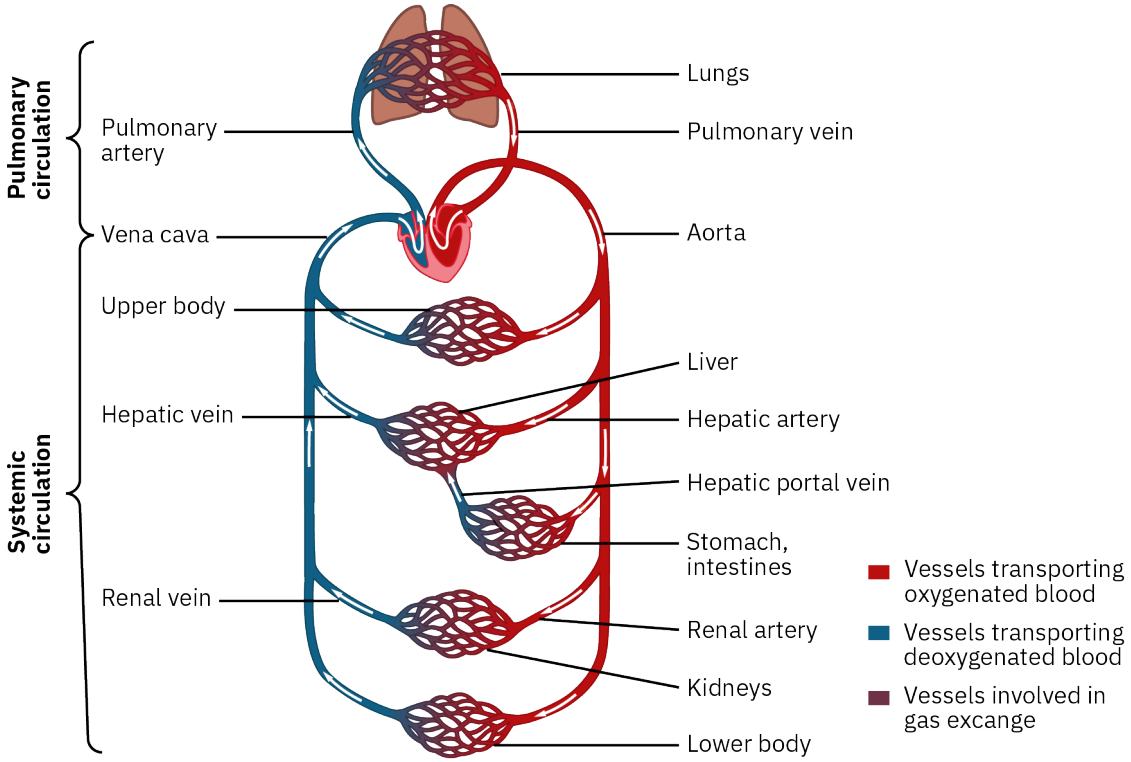


FIGURE 16.3 The pulmonary circuit moves blood from the right side of the heart to the lungs and back to the heart. The systemic circuit moves blood from the left side of the heart to the head and body and returns it to the right side of the heart. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Systemic Arterial Pressure

Systemic arterial pressure is pressure measured using a sphygmomanometer (blood pressure cuff) and is commonly just referred to as blood pressure. It is the pressure that can be measured in the arteries. It is dependent on both **cardiac output** (the amount of blood pumped from the left ventricle per unit of time) and **systemic vascular resistance** (the resistance to blood flow within the artery, determined by the arterial diameter, which changes based on physiologic conditions). A higher cardiac output or higher arterial resistance increases systemic arterial pressure. Systemic arterial pressure is measured in millimeters of mercury (mm Hg) and often is communicated in a clinical setting by systolic blood pressure/diastolic blood pressure. Systolic blood pressure is the pressure in the arteries during systole, or ventricular contraction (heart pumping). Diastolic blood pressure is lower and is the pressure in the arteries during diastole, or ventricular filling/relaxation (between each pump).

Mean arterial pressure (MAP) also provides a measure of systemic arterial pressure throughout the cardiac cycle. A typical MAP is 70–100 mm Hg. It is calculated using the following formula:

$$\text{MAP} = \frac{2}{3} \times \text{Diastolic Blood Pressure} + \frac{1}{3} \times \text{Systolic Blood Pressure}$$

Arterial blood pressure facilitates the delivery of nutrients and oxygen to the tissues (perfusion) and, as such, is highly regulated. It must be high enough to maintain perfusion, but chronically high blood pressure has both acute and chronic risks.

Regulation of blood pressure occurs through several interdependent mechanisms. A summary of these mechanisms follows:

- *Baroreceptor reflex:* Baroreceptors function as sensors and can sense changes in blood pressure and blood volume. When baroreceptors sense low blood pressure or volume, they cause compensatory physiologic changes in the body to raise the blood pressure or volume. One of these changes is net increased activity of the sympathetic nervous system (the fight-or-flight response mediated by epinephrine and norepinephrine, leading to increased vasoconstriction and, thus, increased arterial pressure). This immediate effect on the sympathetic nervous system is responsible for maintaining blood pressure upon abrupt changes, such as when someone moves from a recumbent position to standing quickly. Other changes that occur in response to

baroreceptor activation are increased secretion of the hormones renin and aldosterone, which increase circulating volume.

- *Antidiuretic hormone:* Antidiuretic hormone (also known as vasopressin) is released in response to low blood pressure (among other triggers). It facilitates passive water reabsorption in the collecting duct of the kidneys, which increases circulating blood volume and cardiac output and thus systemic arterial pressure. Vasopressin can be administered therapeutically to maintain blood pressure in clients with vasodilatory or septic shock (Evans et al., 2021).
- *Renin-angiotensin-aldosterone system (RAAS):* In the RAAS system, renin facilitates the conversion of angiotensinogen to angiotensin I. Angiotensin I is converted to angiotensin II by angiotensin-converting enzyme (ACE). Angiotensin II causes vasoconstriction, which 1) increases vascular resistance and thus systemic arterial pressure; 2) increases the amount of sodium and water resorption in the kidneys, which increases circulating blood volume, cardiac output, and thus systemic arterial pressure; 3) increases secretion of antidiuretic hormone, described above; and 4) increases the release of aldosterone. Aldosterone is a hormone that upregulates a pump called the sodium-potassium-ATPase. This pump facilitates the transport of sodium (and water) back into the body, which increases blood volume and cardiac output and thus systemic arterial pressure. Aldosterone also causes increased potassium excretion. Many drugs work on the RAAS system to regulate blood pressure and will be discussed in Heart Failure Drugs. These include angiotensin-converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARBs), and aldosterone antagonists such as spironolactone (Unger et al., 2020).

Normal blood pressure is generally less than 120/80 mm Hg (American Heart Association, 2022). Hypertension refers to clients with blood pressure greater than 130–140/80–90 mm Hg (Unger et al., 2020; Whelton et al., 2018), and hypotension refers to clients with low blood pressure (systolic blood pressure less than 90 mm Hg). Any blood pressure higher than 180/120 mm Hg is considered a hypertensive crisis and requires immediate medical attention to prevent or mitigate acute end-organ damage (Whelton et al., 2018). Antihypertensive and Antianginal Drugs includes a detailed description of hypertension.

Venous Pressure

Venous pressure is the pressure within the veins. Venous pressure is much lower than arterial pressure. While arterial blood is driven by pumping of the muscular heart (left ventricle), venous circulation is powered by contraction of the muscles surrounding the veins that squeeze the blood through. Veins have one-way valves that direct blood toward the heart and prevent backflow. Veins deliver deoxygenated blood to the right atrium, which is then pumped to the pulmonary circuit for oxygenation, returned to the heart, and then is pumped throughout the body again. A normal central venous pressure (measured using an invasive technique in the vena cava) is 8–12 mm Hg (Shah & Louis, 2022).

TRENDING TODAY

Million Hearts

The Live to the Beat (https://openstax.org/r/millionhearts) campaign is a collaboration of Million Hearts and the CDC Foundation with the goal of reducing cardiovascular disease among Black adults ages 35 to 54. The website contains many resources including educational videos, inspiring stories, social media graphics, and printable materials that encourage people to reduce their cardiovascular risk factors such as hypertension.

16.2 Pumping Action of the Heart

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 16.2.1 Discuss the pumping action of the heart.
- 16.2.2 Describe the cardiac cycle.
- 16.2.3 Explain hemodynamics

An Introduction to the Pumping Action of the Heart

The heart pumps in a complex and coordinated cycle to move blood between the chambers of the heart, the lungs, and the associated blood vessels.

Ventricular systole (or just systole if not specified) refers to the active pumping or contraction of the ventricles. The contraction of the heart muscle increases pressure within the ventricles. When the pressure in the ventricles exceeds the pressure in the attached blood vessel (right ventricle: pulmonary artery; left ventricle: aorta), it causes the connected semilunar valve to open, and blood is ejected into the vessel. On the right side of the heart, contraction of the right ventricle during systole causes the pulmonary valve to open, and blood then flows through the open valve into the pulmonary artery. On the left side of the heart, contraction of the left ventricle during systole causes the aortic valve to open, and blood then flows through the open valve and into the aorta. After systole, the ventricular heart muscle relaxes, and the chamber refills with blood. This phase of relaxation and filling is referred to as *ventricular diastole*, or just **diastole**.

Note: When reading the terms *systole* and *diastole*, it is reasonable to assume this is referring to ventricular systole and diastole. Typically, atrial systole and atrial diastole will be noted as such.

Generally, the right and left sides of the heart pump simultaneously, with the two ventricles contracting nearly in tandem. While the ventricles are contracting during ventricular systole, both of the atria are filling with blood (which will next travel to the associated ventricles during ventricular diastole or filling). The atria undergo systole (contraction) and diastole (relaxation/filling) as well.

The left and right sides of the heart have similar functions but vary considerably in their pumping ability. For example, the left ventricle must pump blood into the high-pressure arterial circulation (~90 mm Hg), whereas the right ventricle pumps blood only through the low-pressure pulmonary circulation (8–20 mm Hg). Accordingly, the left ventricle must work harder as compared to the right. When clients experience heart failure, it is commonly an issue with the left ventricle's ability to pump (e.g., heart failure with reduced ejection fraction; see Heart Failure Drugs). One way to alleviate heart failure symptoms is by reducing systemic arterial pressure with drugs, making it easier for the left ventricle to pump blood out.

Cardiac Cycle

The cardiac cycle is a complex cycle that relies on pressure gradients and valves to direct blood through the heart and pulmonary circuit and into the systemic circulation. Blood flows from areas of higher pressure to areas of lower pressure based on pressure gradients, or differences in pressure among different spaces. The phases of the cardiac cycle are systole (contraction/pumping) and diastole (relaxation/filling), as described in the previous section. This section will follow the path of blood through the heart, pulmonary, and circulatory system (see Figure 16.4):

- *Right atrial diastole (i.e., filling the right atrium):* Blood enters the heart via the superior and inferior venae cavae. Blood flows directly into the right atrium. The right atrium fills with blood, and during this time the tricuspid valve is closed. Concurrently, the right ventricle is pumping a different portion of blood.
- *Right atrial systole/right ventricular diastole (i.e., pumping blood from the right atrium to fill the right ventricle):* The atria are then triggered to contract by the electrical conduction system of the heart. During atrial contraction (known as atrial systole or atrial kick), the pressure increases within the cavity of the atrium and eventually exceeds the pressure in the right ventricle. This causes the tricuspid valve to open, and blood flows into the right ventricle (ventricular diastole). The pulmonary valve is closed.
- *Right ventricular systole (i.e., pumping blood from the right ventricle to the pulmonary artery):* The ventricles are triggered to contract by the electrical conduction system of the heart, starting ventricular systole. During ventricular systole, the pressure in the ventricle increases and becomes greater than the pressure within the pulmonary artery, causing the pulmonary valve to open. Blood flows into the pulmonary artery and then the lungs for gas exchange. Concurrently, atria are refilled with a new portion of blood.
- *Left atrial diastole (i.e., filling the left atrium):* Blood returns from the lungs via the pulmonary vein and flows directly into the left atrium. The mitral valve is closed.
- *Left atrial systole/left ventricular diastole (i.e., pumping blood from the left atrium to fill the left ventricle):* The atria are then triggered to contract by the electrical conduction system of the heart. During atrial contraction (known as atrial systole or atrial kick), the pressure in the left atrium eventually exceeds that of the left

ventricle. This causes the mitral valve to open, and blood flows into the left ventricle (ventricular diastole). The aortic valve is closed.

- *Left ventricular systole (i.e., pumping blood from the left ventricle to the body):* The ventricles are triggered to contract by the electrical conduction system of the heart, starting ventricular systole. During ventricular systole, contraction of the left ventricle causes the pressure within the cavity to increase. It eventually exceeds the pressure within the aorta, and the aortic valve opens. Blood flows into the aorta and then the lungs for gas exchange. Concurrently, the atria are refilling with a new portion of blood.
- *Systemic circulation:* Oxygenated blood is delivered to the tissues via arteries and capillaries, and deoxygenated blood returns to the heart via veins and the venae cavae to restart the cycle with right atrial diastole.

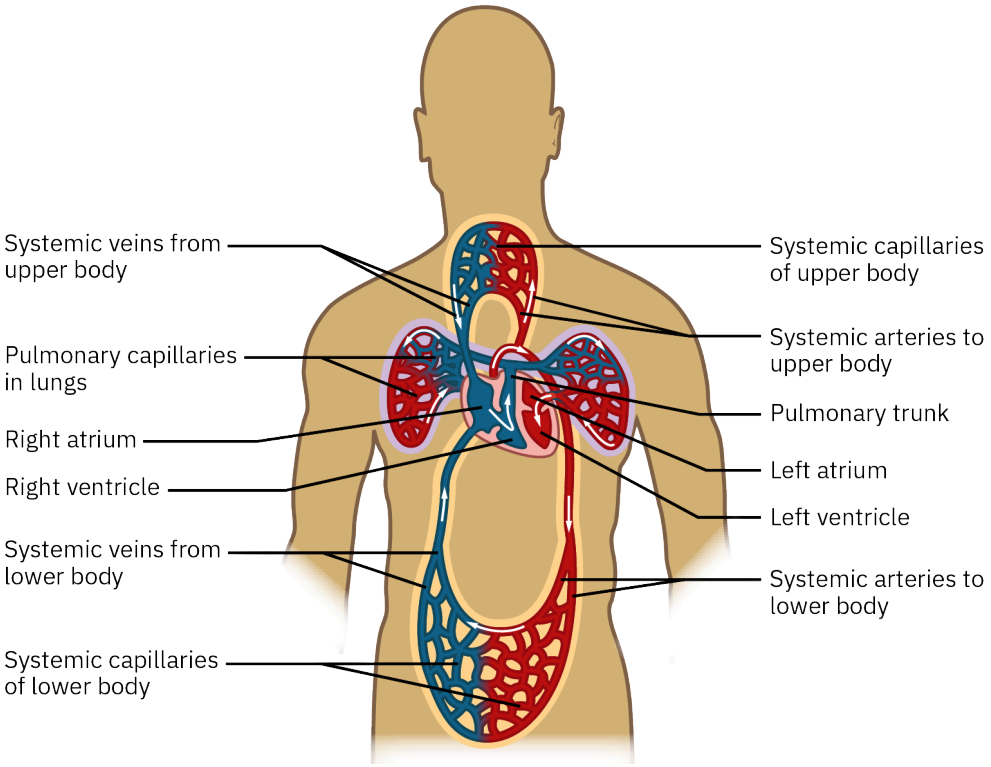


FIGURE 16.4 The colors in this diagram reflect the dual system of blood circulation. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

LINK TO LEARNING

Follow the Path of Blood Through the Heart

Access multimedia content (https://openstax.org/books/pharmacology/pages/16-2-pumping-action-of-the-heart)

The National Heart, Lung, and Blood Institute provides a video that shows the path of blood through the heart during the cardiac cycle.

Cardiac Output and Hemodynamics

Cardiac output is the amount of blood being pumped from the heart into the systemic circulation per unit of time. Cardiac output, systemic vascular resistance, and mean arterial pressure are related by the following formula:

$$\text{Mean Arterial Pressure} = \text{Cardiac Output} \times \text{Systemic Vascular Resistance}$$

As shown by this formula, cardiac output contributes to the mean arterial pressure. Cardiac output is dependent on the heart rate (the number of times the ventricle contracts per unit of time) and stroke volume (the volume of blood ejected with each contraction). The stroke volume (and thus cardiac output) is dependent on multiple variables:

- **Preload**: This is the volume of blood that fills the left ventricle at the end of diastole. A higher preload leads to a higher stroke volume. Preload is sometimes referred to as left ventricular end diastolic volume or measured by left ventricular end diastolic pressure because pressure and volume correlate. Preload is dependent on the volume of circulating blood and the degree of venous vasoconstriction. A higher circulating blood volume or less venous vasoconstriction increases preload. Diuretics are drugs that decrease circulating blood volume, thus decreasing preload.
- **Afterload**: This is the amount of systemic pressure the heart must overcome to eject blood during systole. Higher afterload decreases stroke volume. Drugs that decrease systemic vascular resistance, such as antihypertensive medications, decrease afterload.
- **Contractility**: Cardiac contractility refers to the strength of the force of left ventricular contraction. Increased activation of the sympathetic nervous system increases cardiac contractility via the actions of epinephrine and norepinephrine. Ischemia can decrease cardiac contractility. Increased calcium levels can increase cardiac contractility. Various drugs can affect myocardial contractility. A class of drugs called inotropes increase cardiac contractility. Some drugs can actually decrease cardiac contractility as a side effect.

16.3 Conduction of Electrical Impulses

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 16.3.1 Outline the electrical conduction system of the heart.
- 16.3.2 Discuss automaticity, conductivity, and myocardial contractility.
- 16.3.3 Explain the importance of electrocardiography as it relates to the electrical conduction system of the heart.

Electrical Conduction System of the Heart

The heart's rate and rhythm are controlled by a conduction system that uses electrical impulses to cause the heart to pump blood throughout the body.

The conduction system of the heart generates and carries the impulses that initiate and regulate the heart rate. The heart rate can be measured by palpation of the pulse on an artery such as the radial artery (known as a peripheral pulse) or by auscultation on the chest at the apex of the heart (known as an apical pulse). Each beat correlates with ventricular contraction. The pacemaker of the heart is the sinoatrial (SA) node in the atrium, which possesses **automaticity**, or the ability to spontaneously generate an electrical impulse that initiates the heartbeat. The impulse from the sinoatrial node is conducted through a specialized pathway down through the ventricles and eventually reaches the cardiac muscle cells, or cardiac myocytes, to trigger coordinated contraction of the heart chambers at their respective times in the cardiac cycle.

LINK TO LEARNING

The Conduction System of the Heart

Access multimedia content (https://openstax.org/books/pharmacology/pages/16-3-conduction-of-electrical-impulses)
The National Heart, Lung, and Blood Institute provides a video with information about the heartbeat and a video with an image of the conduction system, including the pacemaker of the heart.

The origination of the impulse from the sinoatrial node in the atrium and the pathway of conduction is what leads to a normal heart rate (60–100 beats per minute) and rhythm, which is called normal sinus rhythm.

Impulse generation and conduction work through **depolarization** of the cells in the conduction system. Depolarization is the cell membrane potential increasing or becoming more positive as compared to its surroundings. The cells of the cardiac conduction system maintain a negative resting voltage (i.e., ionic charge), also known as **membrane potential**. An **action potential** describes rapid depolarization of the cell, followed by repolarization (the cell membrane potential decreasing back to the resting voltage).

The mechanisms for depolarization and repolarization vary, but in general, they rely on electrolytes or electrically

charged ions. Positively charged ions such as sodium (Na^+), potassium (K^+), or calcium (Ca^{2+}) *entering* the cell make it less negative and mediate repolarization. Ions or substances entering the cell is referred to as influx. Positively charged ions such as Na^+, K^+, or Ca^{2+} *leaving* the cell make it more negative and mediate repolarization. Ions or substances leaving the cell is referred to as efflux. Given how central electrolytes are to cardiac function and the electrical conduction system of the heart, it is important to monitor clients' blood levels to ensure they are sufficient. Hypokalemia, or a low potassium blood level, is a risk factor for dysrhythmias and should be avoided.

Automaticity

Automaticity describes a cell's ability to spontaneously generate an electrical impulse that allows it to function as the pacemaker of the heart. In a healthy heart, the sinoatrial node has an intrinsic rate of spontaneous impulses of 60–100 beats per minute (Kashou et al., 2022). The atrioventricular node, **bundle of His**, and **Purkinje fibers** also possess automaticity; however, their lower rate of spontaneous impulses (varying at 20–40 beats per minute) are suppressed by the higher rate of the sinoatrial node. In a healthy heart, the atrioventricular node, bundle of His, and Purkinje tissues do not demonstrate their automaticity.

Automaticity in the pacemaker cells is a result of a spontaneous current, called the pacemaker or "funny" current. This current spontaneously and slowly raises the membrane potential of the pacemaker cell until it reaches a threshold level. At the threshold, an action potential is triggered. In pacemaker cells, the rapid depolarization phase of the action potential is mediated by calcium influx, and repolarization is mediated by potassium efflux (i.e., leaving the cell).

Conductivity

The cells of the cardiac conduction system receive the spontaneous impulses from the sinoatrial node and conduct, or carry, the signal through the atrioventricular node and then the bundle of His, which then splits into the left and right bundle branches. Each bundle branch gives rise to Purkinje fibers, which conduct the impulse into the cardiac muscle to facilitate contraction. Depolarization spreads from cell to cell via gap junctions, which are membranous connections between the cells. Figure 16.5 depicts the structures of the cardiac conduction system.

Conductivity is mediated by action potentials. The resting membrane potential is negative. During conduction, rapid depolarization is mediated by sodium influx. The cell remains depolarized for a time period while calcium influx (through L-type calcium channels) and potassium efflux are relatively balanced, and then repolarization occurs via potassium efflux. A refractory period follows depolarization when the sodium channels that usually mediate depolarization are inactive. During the refractory period, the cell cannot be depolarized until the refractory (or inactive) period is over.

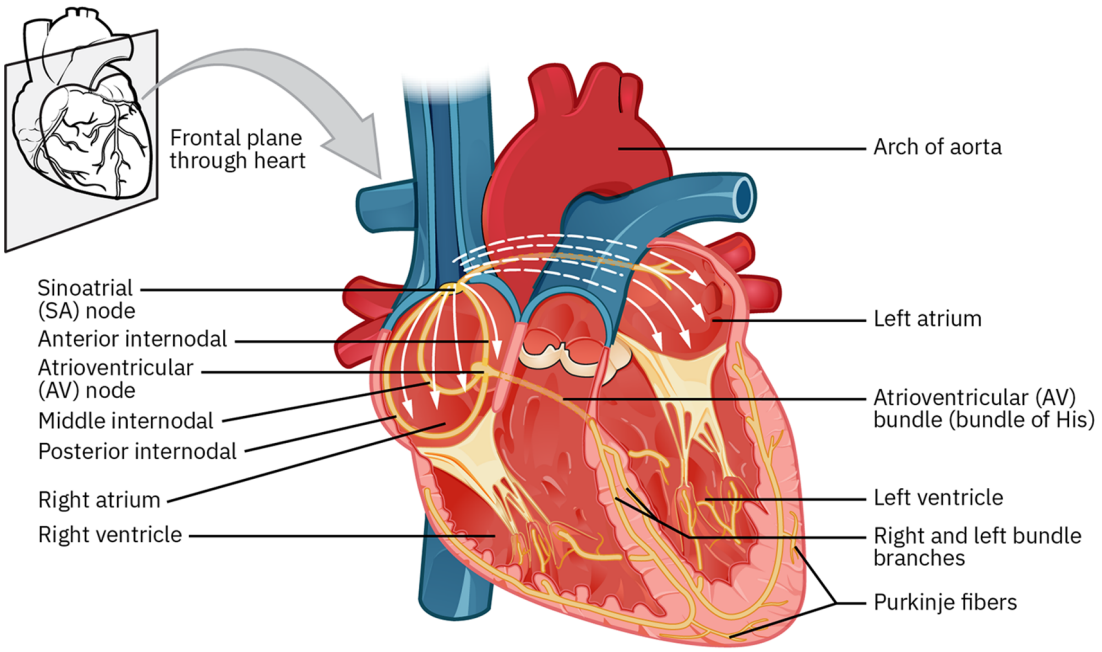


FIGURE 16.5 This image of the heart shows the conduction tissue and pathway. Specialized conducting components of the heart include the sinoatrial node, the internodal pathways, the atrioventricular node, the atrioventricular bundle, the right and left bundle branches, and the Purkinje fibers. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Myocardial Contractility

The cardiac myocytes receive the electrical impulse from the conduction tissue and are stimulated to contract in a process called excitation-contraction coupling. During an action potential, calcium enters the cardiac myocyte via L-type calcium channels and then interacts with receptors called ryanodine receptors on the sarcoplasmic reticulum, which is a tubular structure found within the cell that stores calcium. This causes release of comparatively massive amounts of calcium into the cytoplasm from the sarcoplasmic reticulum in a process called *calcium-induced calcium release*. The high levels of calcium cause downstream contraction of the cardiac myocytes.

Myocardial contraction occurs due to the interaction of two proteins called actin and myosin that each form separate long filaments. At rest, the interaction between actin and myosin is blocked by a protein called tropomyosin. Calcium causes changes in tropomyosin (via a protein called troponin), rendering it unable to inhibit the interaction of actin and myosin. Uninhibited, filaments of actin and myosin attach and slide past each other, which is the basis for myocyte contraction.

LINK TO LEARNING

Excitation-Contraction Coupling

Access multimedia content (https://openstax.org/books/pharmacology/pages/16-3-conduction-of-electrical-impulses)

StrongMed provides a video summarizing the process of excitation-contraction coupling in the heart.

Electrocardiography

Electrocardiography (EKG or ECG) is a common diagnostic tool that allows health care professionals to monitor various aspects of the client's heart including rate, rhythm, and the presence of ischemia. It is also used for monitoring medications. In a typical ECG, 12 leads are placed on the client's chest and limbs in a specific orientation that allows them to detect the electrical activity of the cardiac conduction system. The client's heart rate and rhythm are recorded visually through waves and intervals, which represent various aspects of conduction through the heart. Figure 16.6 shows an example of an electrocardiogram and its components.

Waveforms

When the cardiac electrical impulse is conducted in the direction of a lead, it creates an upward deflection; when traveling away, it causes a downward deflection. These are called **waveforms**. A segment on an ECG is the space between two waves and does not include a waveform. An interval, on the other hand, includes the space between two waves *and* a waveform. The final ECG represents the summation of the impulses from all leads. This creates a pattern of waves for each cardiac cycle (heartbeat) that repeats for the duration of monitoring.

In a healthy heart, each cardiac cycle consists of a P wave, followed by a QRS complex (a combination of a Q wave, R wave, and S wave), and lastly a T wave. The P wave represents atrial depolarization, which is when the electrical impulse travels from the sinoatrial node through the atria to cause atrial contraction. After the P wave, the tracing comes back to baseline as the signal is transmitted through the AV node. The QRS complex represents ventricular depolarization, which is the electrical conduction signal that causes ventricular contraction or ventricular systole. Finally, the T wave represents ventricular repolarization. (Atrial repolarization is not visualized.) The interval from the beginning of the QRS complex to the end of the T wave is called the QT interval. Segments are the regions between two waves.

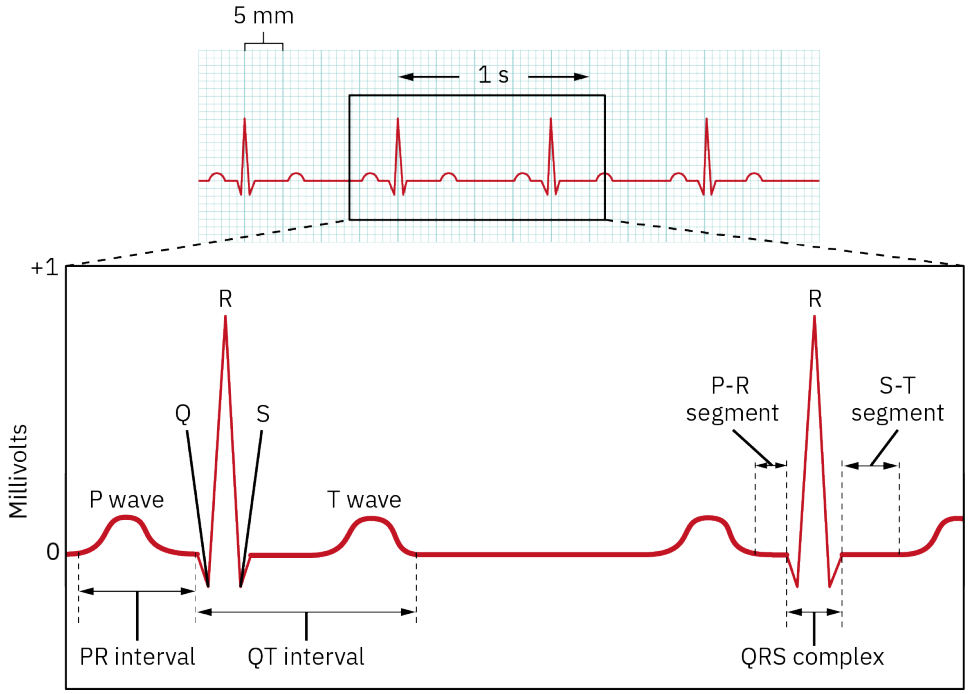


FIGURE 16.6 A normal electrocardiogram tracing shows the P wave, QRS complex, and T wave. Also indicated are the PR, QT, QRS, and ST intervals, plus the P-R and S-T segments. (credit: modification of work from *Anatomy and Physiology* 2e. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Dysrhythmias

Normal sinus rhythm is the normal rhythm of a healthy heart. This describes the scenario where the sinoatrial node causes the heart to beat at 60–100 beats per minute and at regular intervals (equal time between each heartbeat or ventricular contraction). On the electrocardiogram of a client in normal sinus rhythm, every P wave is followed by a QRS complex, which is followed by a T wave. **Dysrhythmias** describe when there is a problem with the heart rate and/or rhythm. They are also known as *arrhythmias*.

If the heart rate is too fast, it is known as tachycardia. If the heart rate is too slow, it is known as *bradycardia*. If the heart rhythm is irregular, it can be described as regularly irregular, meaning the time between heartbeats varies in a pattern, or irregularly irregular, meaning the time between heartbeats varies without any identifiable pattern. Dysrhythmias can occur when another part of the heart acts as the pacemaker or if conduction of the current occurs through a pathway other than the standard pathway described previously. For more about common dysrhythmias encountered in clinical practice, see Anti-Dysrhythmic Drugs.

Chapter Summary

This chapter focused on an introduction to the cardiovascular system and laid the foundation for cardiovascular pharmacology. The structure and anatomy of the cardiovascular system were described. The heart consists of four chambers: the two upper chambers (atria) and the two lower chambers (ventricles). The heart contains valves that direct blood flow and prevent backflow of blood through the heart. The heart is supplied with blood by the coronary arteries. Arteries carry oxygenated blood away from the heart to the body, and veins carry deoxygenated blood back to the heart from the body. Gas exchange occurs in the tissues via capillaries.

The pumping action of the heart and the cardiac cycle were also discussed. Systole is the contraction of the heart chamber for pumping, and diastole is relaxation of the heart chamber for filling. The venae cavae deliver deoxygenated blood from the tissues to the right atrium, then the blood moves to the right ventricle, which pumps the deoxygenated blood to the pulmonary circuit for oxygenation. Oxygenated blood then returns to the left atrium, and then the blood moves to the left ventricle. During systole, the left ventricle pumps the blood through the aorta to the tissues for use.

Finally, the conduction system of the heart was described. The conduction system is an electrochemical system that causes the heart to pump in a coordinated manner using movement of ions into and out of cells. The sinoatrial node acts as the pacemaker of the heart and spontaneously generates an impulse that moves through the conduction system, eventually reaching the muscle cells and causing them to contract during systole. The electrocardiogram allows clinicians to monitor the heart rate and rhythm in a noninvasive manner and can help diagnose dysrhythmias, or abnormal heart rhythms.

Key Terms

action potential rapid depolarization of the cell (i.e., the cell membrane potential increasing or becoming more positive as compared to its surroundings) followed by repolarization (i.e., the cell membrane potential decreasing back to the resting voltage)

afterload the amount of systemic pressure that the heart must overcome to eject blood during systole

arteries blood vessels that carry oxygenated blood away from the heart and to the tissues for perfusion; singular, artery

atria the two upper chambers of the heart; singular, atrium

automaticity a process by which a spontaneous action potential forms, allowing a tissue to act as the pacemaker of the heart

bundle of His part of the electrical system of the heart

capillaries small blood vessels that run between arteries and veins and allow oxygen perfusion and nutrient exchange; singular, capillary

cardiac output the amount of blood pumped from the left ventricle per unit of time

contractility the strength of the force of left ventricular contraction

depolarization a process by which a cell's negative baseline resting membrane potential increases and becomes positive

diastole the phase of the cardiac cycle in which a chamber is relaxing or filling

dysrhythmias irregularities in the heart rate or rhythm; singular, dysrhythmia

electrocardiography (EKG, ECG) a common diagnostic tool that allows health care professionals to monitor various aspects of a client's heart including rate, rhythm, or the presence of ischemia.

membrane potential the voltage (i.e., ionic charge) of a cell as compared to its surroundings

preload the volume of blood that fills the left ventricle at the end of diastole

pulmonary arteries the blood vessels that carry deoxygenated blood from the right ventricle to the lungs for gas exchange; singular, artery

pulmonary veins blood vessels that carry oxygenated blood from the lungs back to the left atrium of the heart; singular, vein

Purkinje fibers special muscle cells that allow coordinated contraction of the heart

systemic vascular resistance the resistance to blood flow within the artery, determined by the arterial diameter

systole the phase of the cardiac cycle in which a chamber is contracting or pumping

veins blood vessels that carry deoxygenated blood back to the heart

ventricle one of the two lower chambers of the heart

waveforms the upward and downward deflection on an electrocardiogram

Review Questions

1. The nurse is watching a client's cardiac monitor. The nurse recognizes that the QRS complex represents which phase of the cardiac cycle?
   a. Atrial depolarization
   b. Atrial repolarization
   c. Ventricular depolarization
   d. Ventricular repolarization

2. Which of the following cardiac chambers pumps blood to the pulmonary artery and thus is prone to failure in clients with pulmonary arterial hypertension?
   a. Right ventricle
   b. Left ventricle
   c. Right atrium
   d. Left atrium

3. The nurse is caring for a client following a myocardial infarction. Which blood vessel does the nurse explain is blocked?
   a. Aorta
   b. Coronary artery
   c. Vena cava
   d. Coronary vein

4. A client is being sent to the cardiac catheterization laboratory after an acute myocardial infarction. During the procedure, a physician will puncture and enter the femoral artery to gain access to various heart structures. Which of the following differentiates arteries like the femoral artery from veins?
   a. Arteries have a lower blood pressure in comparison to veins.
   b. Arteries carry deoxygenated blood back to the heart to be pumped to the pulmonary circuit.
   c. Arteries are lower risk during a puncture in comparison to veins.
   d. Arteries carry oxygenated blood to the body for use by the tissues.

5. The left ventricle pumps blood from the heart to the aorta for use by the body. Which of the following processes occurs nearly simultaneously with left ventricular systole?
   a. Right atrial systole
   b. Right ventricular systole
   c. Right ventricular diastole
   d. Excitation of the sinoatrial node

6. Which of the following carries an electrical signal from the atria to the ventricles in the healthy heart?
   a. Atrioventricular node
   b. Sinoatrial node
   c. Purkinje fibers
   d. Bundle of His

7. Which of the following terms describes the ability of cardiac tissue to act as the pacemaker of the heart?
   a. Membrane potential
   b. Conductivity
   c. Automaticity
   d. Action potential

8. A client is admitted to the hospital with dizziness and shortness of breath. The provider orders an ECG. Which of the following can be diagnosed based on the results of the ECG?
   a. Dysrhythmia

b. Atrial diastole
c. Heart failure with reduced ejection fraction
d. Left ventricular systole

9. The nurse is teaching a group of cardiac rehab clients about the electrical conduction of the heart. What statement made by a client best indicates the teaching is effective?
a. "The sinoatrial node is a specialized bundle of nerve tissue that slows the electrical impulse."
b. "The sinoatrial node is a specialized bundle of nerve tissue that causes ventricular contraction."
c. "The sinoatrial node is a specialized bundle of nerve tissue that repolarizes the ventricular myocardium."
d. "The sinoatrial node is a specialized bundle of nerve tissue in the right atrium called the pacemaker of the heart."

10. A client is admitted with bradycardia detected by an ECG. Which statement describes bradycardia?
a. Heart rate greater than 100 beats per minute
b. Heart rate greater than 60 beats per minutes
c. Heart rate less than 100 beats per minute
d. Heart rate less than 60 beats per minute

CHAPTER 17
Antidysrhythmic Drugs

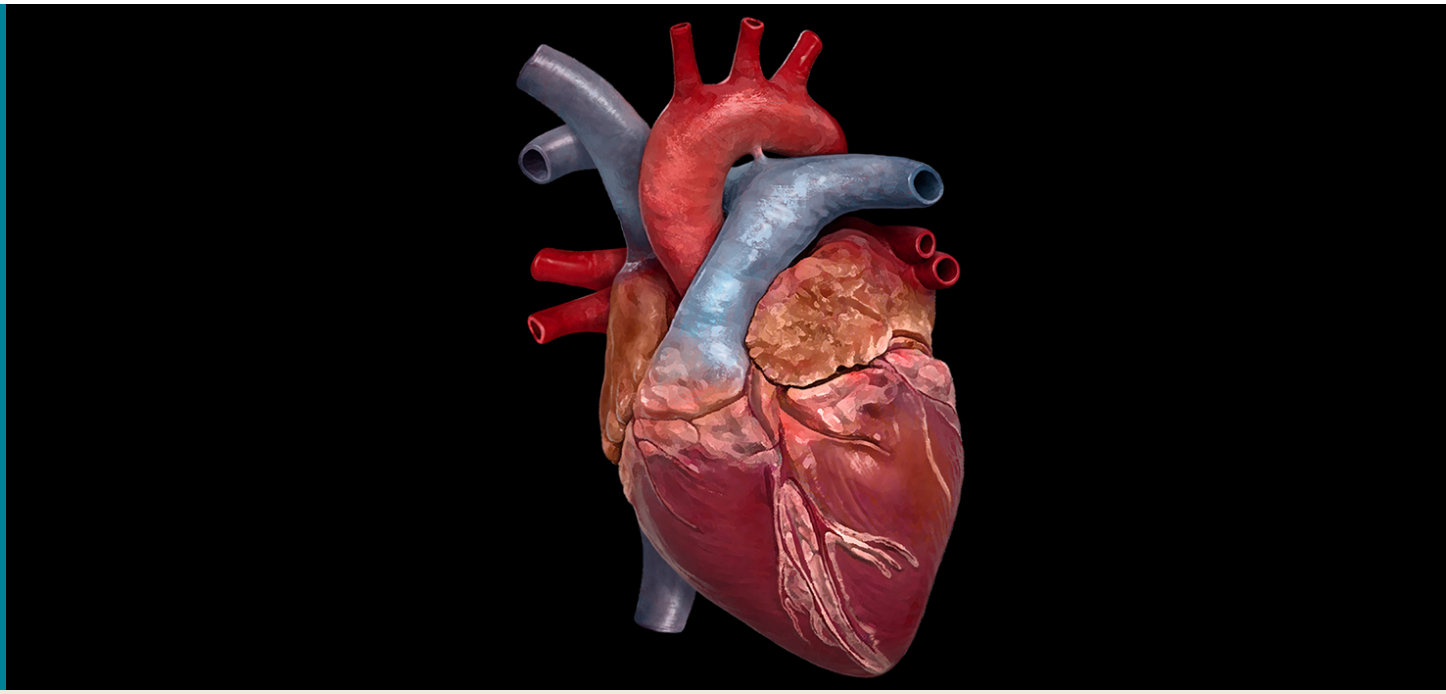


FIGURE 17.1 The heart is the primary organ of the cardiovascular system, controlling circulation and blood flow for the entire body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Normal sinus rhythm is the normal rhythm of a healthy heart. In this rhythm, the sinoatrial (SA) node causes the heart to beat at 60–100 beats per minute and at regular intervals (equal time between each heartbeat or ventricular contraction). The impulse from the SA node is conducted across the atria and then follows a specialized pathway through the atrioventricular (AV) node and ventricles, eventually reaching the cardiac myocytes (muscle cells) to trigger coordinated contraction of the heart chambers at their respective times in the cardiac cycle. On the electrocardiogram (ECG/EKG) of a client in normal sinus rhythm, every P wave is followed by a QRS complex, which is followed by a T wave. Introduction to the Cardiovascular System provides an overview of the cardiac conduction system that facilitates the heart rate and rhythm.

The heart rate and rhythm are regulated by a balance of sympathetic and parasympathetic input. *Sympathetic input* is the "fight or flight response" mediated by catecholamines such as epinephrine at beta-1 receptors in the heart. Stimulation of beta-1 receptors results in increased cardiac contractility (strength of contraction) and chronotropy (effect on heart rate). Parasympathetic input is often referred to as "rest and digest" and affects the heart through vagal innervation of the SA and AV nodes. Increased vagal tone leads to decreased heart rate and electrical conduction. Various conditions can interfere with heart rate and rhythm leading to serious and potentially life-threatening conditions. This chapter will explore how different medications affect the heart to treat these conditions.

17.1 Introduction to Dysrhythmias

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 17.1.1 Describe specific cardiac dysrhythmias and their significance to cardiac function.
- 17.1.2 Discuss the principles of managing dysrhythmias to improve cardiac functioning.

Dysrhythmias

Dysrhythmias, also known as arrhythmias, occur when there is abnormal automaticity (spontaneous impulse generation) or abnormal conduction that results in a problem with the heart rate and/or rhythm. Medications address dysrhythmias by manipulating the electrolytes and other receptors involved in the cardiac conduction system to either treat the manifestations of the underlying arrhythmia or restore a normal heart rate, suppress the dysrhythmia, and thus restore normal sinus rhythm in a process known as **cardioversion**. When cardioversion is accomplished via drug administration, may be referred to as *chemical* cardioversion.

Dysrhythmias can be classified in multiple ways. One way is according to the ventricular contraction rate, or heart rate. A heart rate less than 60 beats per minute is considered **bradycardia**. Bradycardia can occur due to the SA node incorrectly pacing too slowly or to the AV node conducting incorrectly, leading to AV block. Bradycardia can lead to problems because it decreases cardiac output, which is affected by both stroke volume and heart rate. A heart rate greater than 100 beats per minute is called **tachycardia**. Tachycardia can further be categorized as **supraventricular tachycardia** (the stimulus physically originates above the ventricle but not from the sinus node) or **ventricular tachycardia** (the origin of the stimulus is physically located in the ventricle). Tachycardia is problematic because at very high heart rates, the ventricles do not have enough time to fill with an adequate amount of blood in between contractions. Thus, the stroke volume and cardiac output are both decreased. Tachycardia also increases the workload of the heart and can lead to a type of heart failure called tachycardia-induced cardiomyopathy.

Sinus Bradycardia

In sinus bradycardia, although the heart rate is less than 60 beats per minute, the rhythm is regular, and the SA node acts as the pacemaker for the heart. Aside from the slow heart rate, there is no other problem with conduction. On an ECG, every P wave is followed by a QRS complex, which is followed by a T wave.

Sinus Tachycardia

In sinus tachycardia, although the heart rate exceeds 100 beats per minute, the rhythm is regular, and the SA node acts as the pacemaker for the heart. Aside from the rapid heart rate, there is no other problem with conduction. Every P wave is followed by a QRS complex, which is followed by a T wave. Sinus tachycardia is often caused by exercise, pain, stress, anxiety, or dehydration.

Atrial Fibrillation

Atrial fibrillation is described as an irregularly irregular rhythm in which multiple areas of the atria generate spontaneous impulses such that the atria quiver at 400–600 beats per minute. Only some of the impulses are conducted through the AV node, resulting in a variable ventricular contraction rate or heart rate. When the heart rate is high, it is called **atrial fibrillation with rapid ventricular response**. Because the atria are quivering because so many impulses are being formed, the individual's ECG will show no distinguishable P waves; however, the baseline will appear wavy due to the presence of "fibrillatory" waves (Figure 17.2).

There are two overall strategies for treating atrial fibrillation: rhythm control and rate control. The aim of rhythm control is to cardiovert and then maintain normal sinus rhythm. Rate control is a strategy that allows the client's rhythm to remain in atrial fibrillation but slows the rate of conduction through the AV node, thereby slowing the ventricular rate/heart rate.

Atrial Flutter

Atrial flutter is a dysrhythmia closely related to atrial fibrillation. The atria quiver at rates of 250–400 beats per minute. As with atrial fibrillation, abnormal impulses are generated in the atria. Commonly, there is 2:1 conduction through the AV node, meaning that for every two impulses from the atria, one conducts through the AV node and leads to ventricular contraction. This process commonly leads to a ventricular rate of approximately 150 beats per minute (assuming an average atrial rate of 300 beats per minute). It is noteworthy that the conduction is not always

2:1; it may be 3:1, 4:1, or 5:1. As in atrial fibrillation, there are no typical P waves on the ECG of a client with atrial flutter. Instead, there are "flutter waves" in a characteristic sawtooth pattern between QRS complexes.

Premature Ventricular Contraction

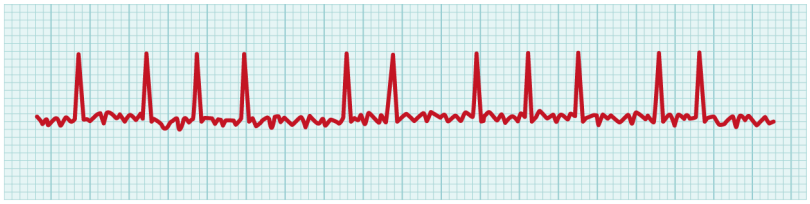
A premature ventricular contraction (PVC) represents the ventricle contracting earlier than it should during the cardiac cycle due to a spontaneous impulse from the Purkinje fibers (rather than from an impulse carried from the SA node).

Ventricular Tachycardia

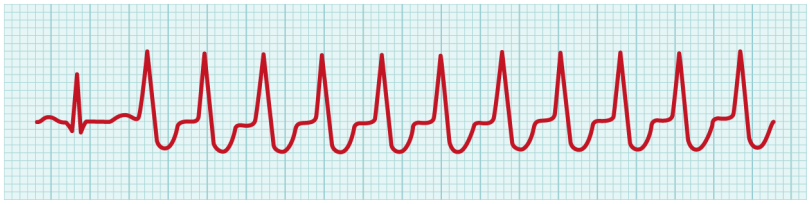
When multiple PVCs occur consecutively, it is known as ventricular tachycardia. Sustained ventricular tachycardia (lasting more than 30 seconds) can be serious and cause hemodynamic compromise necessitating advanced cardiac life support. Ventricular tachycardia can occur due to abnormalities of electrolytes such as magnesium or potassium or to myocardial ischemia (oxygen deprivation in the heart muscle). It can devolve into ventricular fibrillation, described next. On an ECG, ventricular tachycardia has multiple wide QRS complexes (Figure 17.2). **Torsade de pointes** is a dangerous ventricular tachycardia associated with medications that prolong the QT interval (the time it takes the heart to contract and recover).

Ventricular Fibrillation

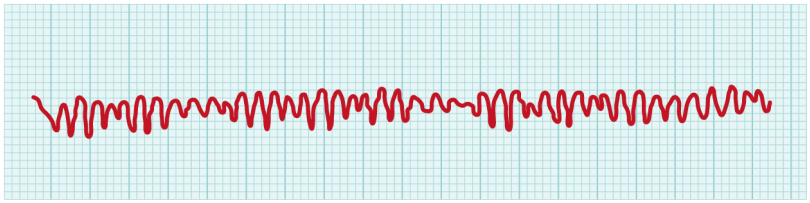
Ventricular fibrillation is a medical emergency that necessitates advanced cardiac life support (ACLS). This is another ventricular arrhythmia, meaning it originates from spontaneous impulses from the Purkinje fibers (rather than from an impulse carried from the SA node), causing the ventricles to quiver erratically rather than pump, which, in turn, causes cardiac arrest. On an ECG, ventricular fibrillation appears as multiple and varied wide complexes, without any pattern or discernable P waves, QRS complexes, or T waves (Figure 17.2).



Atrial fibrillation



Ventricular tachycardia



Ventricular fibrillation

FIGURE 17.2 Some examples of ECG abnormalities include atrial fibrillation, ventricular tachycardia, and ventricular fibrillation. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Asystole

In asystole, the heart has no electrical activity and thus does not pump. This is a medical emergency that necessitates advanced cardiac life support. On an ECG, asystole has no waveforms, which is why it is often informally called "flatlining."

Pulseless Electrical Activity

In pulseless electrical activity (PEA), the client's ECG shows electrical activity (possibly even sinus rhythm);

however, it does not lead to ventricular contraction, and the client does not have a pulse. This is a medical emergency that requires advanced cardiac life support.

Management of Cardiac Dysrhythmias

Management of cardiac dysrhythmias is extremely diverse and is based on client-specific factors, the particular dysrhythmia being treated, the setting of the dysrhythmia (acute vs. chronic), and the client's comorbidities. Many therapies for dysrhythmias are managed by an electrophysiologist, a cardiologist who specializes in the treatment of dysrhythmias.

Nonpharmacologic Management

Nonpharmacologic management of dysrhythmias depends on the specific dysrhythmia being treated and the clinical scenario. Lifestyle changes, procedures, and vagal maneuvers are all examples of nonpharmacologic management that can be attempted, depending on the client. In terms of lifestyle changes, clients can avoid or manage triggers of their arrhythmias. Some lifestyle-related triggers of dysrhythmias include anger, physical activity and exercise, alcohol, caffeine, lack of sleep, and use of illicit stimulant drugs such as cocaine (Groh et al., 2019; National Heart, Lung, and Blood Institute, 2022).

Depending on the specific dysrhythmia and clinical scenario, various procedures, such as an ablation, can be performed to manage an arrhythmia. An ablation uses radiofrequency to create scar tissue, which does not conduct electrical impulses, in the irregular heart tissue that is causing the arrhythmia (El Baba et al., 2020). **Vagal maneuvers** are physical manipulations that can increase parasympathetic activation to treat various arrhythmias. One example of a vagal maneuver is the Valsalva maneuver. The Valsalva maneuver is commonly referred to as "bearing down" and is the process of forced expiration against a closed glottis (Niehues & Klovenski, 2022). Vagal stimulation leads to a decreased rate of pacing from the SA node and decreased conduction through the AV node.

Pharmacologic Management

Antidysrhythmic drugs treat abnormal heart rates and rhythms. They are often classified using the **Vaughan Williams classification system**, which differentiates drugs by their major mechanism of action (Table 17.1). However, this system is far from perfect. Many of the antidysrhythmic drugs have multiple mechanisms of action, so there is overlap among the categories; many drugs do not fit perfectly into a single category. Still, this is the most conventional way to classify the drugs. The categories include:

- Class I: Sodium channel blockers
- Class II: Beta-adrenergic blockers
- Class III: Potassium channel blockers
- Class IV: Calcium channel blockers
- *Unclassified (also called miscellaneous):* Drugs that work by alternative mechanisms

The choice of which antidysrhythmic drug to use is nuanced and requires in-depth knowledge and experience. It is noteworthy that the Institute for Safe Medication Practices considers the majority of antidysrhythmic drugs discussed in this chapter to be high-alert drugs due to their propensity for causing client harm when administered incorrectly. Drugs used in advanced cardiac life support that are not traditional antidysrhythmic medications (such as epinephrine and calcium carbonate) are discussed in Cardiac Emergency and Shock Drugs.

Class	Description	Example Drugs
I	Sodium channel blockers	Quinidine (IA) Procainamide (IA) Disopyramide (IA) Lidocaine (IB) Mexiletine (IB) Flecainide (IC) Propafenone (IC)
II	Beta-adrenergic blockers	Esmolol Metoprolol Atenolol Bisoprolol Nebivolol Betaxolol Acebutolol
III	Potassium channel blockers	Amiodarone Dronedarone Dofetilide Ibutilide Sotalol
IV	Calcium channel blockers	Diltiazem Verapamil
Unclassified	Various mechanisms	Atropine Digoxin Adenosine

TABLE 17.1 **Vaughan Williams Classification of Antidysrhythmic Drugs**

SPECIAL CONSIDERATIONS

Older Adults

The risk of being diagnosed with dysrhythmia skyrockets after age 60. Not only does the risk for dysrhythmias increase, but older adults have a higher risk for concomitant disease states that interfere with the action of antidysrhythmic drugs. For example, beta-adrenergic blockers, quinidine, and procainamide can exacerbate the postural hypotension that is particularly prevalent in older adults, leading to falls. Clients with heart failure (who are usually older adults) can experience exacerbation of their underlying condition when treated with flecainide or sotalol. Furthermore, older clients are more likely to be on multiple medications, increasing the likelihood of experiencing drug interactions. Age-related decreases in metabolic processing and excretion of drugs can increase antidysrhythmic plasma levels, putting these individuals at higher risk for adverse effects. Thus, antidysrhythmic drugs require extra vigilance to prevent harm in the older adult population.

(Source: Curtis et al., 2018)

SPECIAL CONSIDERATIONS

Pediatrics

Pediatric clients may experience arrhythmias that must be treated with antidysrhythmic therapy. Some of this use is off-label. Off-label prescription drug use means that the drug may not be specifically approved for a particular client or diagnosis, but health care providers may choose to use the drug anyway because the potential benefit outweighs the potential risks. In these circumstances, drug dosing and administration may not be standardized. The nurse should consult institutional protocols to avoid medication errors, especially

overdoses.

(Source: Oeffl et al., 2023)

17.2 Class I: Sodium Channel Blockers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 17.2.1 Identify the characteristics of the sodium channel blocker drugs used to treat dysrhythmias.
- 17.2.2 Explain the indications, actions, adverse reactions, and interactions of the sodium channel blocker drugs used to treat dysrhythmias.
- 17.2.3 Describe the nursing implications of the sodium channel blocker drugs used to treat dysrhythmias.
- 17.2.4 Explain the client education related to the sodium channel blocker drugs used to treat dysrhythmias.

Class I antidysrhythmic drugs are known as sodium channel blockers. They block sodium channels in conduction tissue and myocytes. Sodium channels are responsible for the depolarization of cardiac cells, and blocking these channels leads to slower conduction and a longer refractory period between impulses. Class I antidysrhythmic drugs are further broken down into classes IA, IB, and IC.

Class IA drugs cause moderate blockade of sodium channels. They also have an additional mechanism of action and block potassium channels. Blockage of potassium channels leads to a property called **proarrhythmia**, meaning the drugs have a propensity to cause other arrhythmias. Drugs that block potassium channels prolong the QT interval, which increases the risk for torsade de pointes.

Class IB drugs block sodium channels with mild intensity. These drugs are exclusively used for ventricular arrhythmias.

Class IC drugs strongly block sodium channels but do not block potassium channels; thus, they are less proarrhythmic than class IA agents (King et al., 2023).

Various sodium channel antidysrhythmic drugs exist. This chapter will cover the following drugs in more detail: quinidine, procainamide, lidocaine, mexiletine, flecainide, and propafenone.

Quinidine

Quinidine is a class IA antidysrhythmic drug. It is available as an oral immediate-release tablet and an extended-release tablet. These tablets are different salt forms of quinidine; the immediate-release form is quinidine sulfate, and the extended-release form is quinidine gluconate. It is important to note that these are *not* interchangeable.

Quinidine is approved by the U.S. Food and Drug Administration (FDA) for cardioversion of atrial fibrillation and flutter to sinus rhythm and then for maintenance of sinus rhythm after cardioversion. It is also approved for suppression of recurrent ventricular arrhythmias.

Quinidine can easily be confused with quinine; nurses must be careful to avoid mixing up these drugs. Clients should be educated on the potential for diarrhea and contact their provider if this occurs because it can lead to electrolyte abnormalities that can exacerbate arrhythmias. Clients who take quinidine should avoid grapefruit and grapefruit juice because of potential interactions.

Procainamide

Procainamide is a class IA antidysrhythmic drug that is available only in an intravenous form. It is FDA approved for life-threatening ventricular arrhythmias but is used off-label for other arrhythmias as well, including atrial fibrillation. Procainamide is metabolized to N-acetyl procainamide, which is also active.

Lidocaine and Mexiletine

Lidocaine is a class IB antiarrhythmic drug. It has various uses as an anesthetic; however, in terms of dysrhythmias, it is used exclusively for treating ventricular arrhythmias. It can be used both for acute treatment of a primary arrhythmia and in advanced cardiac life support when clients have sudden cardiac arrest due to ventricular

arrhythmias. When used for treating arrhythmias, lidocaine is administered only intravenously.

CLINICAL TIP

Lidocaine

Because lidocaine may cause central nervous system toxicity, the nurse should assess the client frequently. Signs and symptoms to watch for include sedation and irritability (twitching), which could progress to convulsions and respiratory depression/arrest.

SAFETY ALERT

Lidocaine

Lidocaine is available in many formulations, some of which are not suitable for intravenous administration. Lidocaine with epinephrine is one such dosage form. The Institute for Safe Medication Practices (https://openstax.org/r/ismporgresources) reported a death that occurred when a client was administered topical lidocaine with epinephrine instead of the intravenous form of lidocaine with epinephrine, causing fatal cardiac arrhythmias. Lidocaine with epinephrine should never be used as an antidysrhythmic agent.

Mexiletine is like lidocaine in that it is a class IB drug. It is FDA approved for managing ventricular arrhythmias and is available as an oral capsule for long-term use.

Flecainide and Propafenone

Flecainide is a class IC antidysrhythmic drug that is available as an oral tablet. It is used for clients with paroxysmal symptomatic supraventricular tachycardias, including atrial fibrillation and atrial flutter. It can also be used for life-threatening ventricular tachyarrhythmias.

Propafenone is also a class IC drug. It is available as an oral immediate-release tablet and an oral extended-release capsule. It is FDA approved to treat life-threatening ventricular arrhythmias and to prolong time to recurrence of paroxysmal atrial fibrillation/flutter in clients without structural heart disease. Propafenone is used off-label in a technique informally called "pill in a pocket." This technique refers to a scenario in which a client who has symptomatic recurrent paroxysmal atrial fibrillation can keep propafenone on hand and take it as needed when they detect symptoms of atrial fibrillation. The medication will convert them back to sinus rhythm without their needing to visit a health care provider. They do not take the medication daily, just when they need it.

Table 17.2 lists common class I antidysrhythmic drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Quinidine	*Ventricular arrhythmias:* *Quinidine sulfate:* 200–600 mg every 6–12 hours. *Quinidine gluconate:* 324–648 mg every 8–12 hours.
Procainamide	*Ventricular arrhythmias:* *Loading dose:* 100 mg intravenously (IV) every 5 minutes, administered until the arrhythmia is suppressed or 500 mg has been administered. *Maintenance dose:* Typically 50 mcg/min/kg.
Lidocaine (Xylocaine)	*Ventricular arrhythmias (hemodynamically stable):* 1–1.5 mg/kg IV bolus, repeat 0.5–0.75 mg/kg IV bolus every 5–10 minutes; maintenance infusion is 1–4 mg/minute IV.
Mexiletine	*Ventricular arrhythmias:* 150–200 mg orally every 8–12 hours.

TABLE 17.2 **Drug Emphasis Table: Class I Antidysrhythmic Drugs** (sources: https://dailymed.nlm.nih.gov/dailymed/; Al-Khatib et al., 2018, January et al., 2014)

Drug	Routes and Dosage Ranges
Flecainide	*Maintenance of normal sinus rhythm in atrial fibrillation:* 50–200 mg orally every 12 hours.
Propafenone (Rythmol SR)	*Maintenance of normal sinus rhythm in atrial fibrillation:* *Immediate release:* 150–300 mg orally every 8 hours. *Extended release:* 225–425 mg orally every 12 hours.

TABLE 17.2 **Drug Emphasis Table: Class I Antidysrhythmic Drugs** (sources: https://dailymed.nlm.nih.gov/dailymed/; Al-Khatib et al., 2018, January et al., 2014)

Adverse Effects and Contraindications

All sodium channel blockers have some propensity to cause heart blocks; however, the adverse effect profile of sodium channel blockers varies greatly depending on the drug.

Quinidine is associated with many serious risks. Trials have shown increased mortality risk compared with placebo and other antiarrhythmic drugs, and for this reason the drug has a boxed warning (DailyMed, *Quinidine gluconate,* 2021). Quinidine has a high incidence of diarrhea as an adverse effect (greater than 20%). It is hepatotoxic and has been associated with serious liver problems, including granulomatous hepatitis, so it should be used with caution in clients with hepatic impairment. It can be associated with thrombocytopenia and therefore should not be used in clients with baseline thrombocytopenia. In addition to acting as a sodium channel blocker, it blocks potassium channels and prolongs the QT interval, which leads to a proarrhythmic effect. The nurse will need to monitor the client's ECG, complete blood count (CBC), and liver and kidney function.

Many serious risks associated with the use of procainamide have led to several boxed warnings. It has the potential to cause drug–induced lupus erythematosus–like syndrome as well as blood dyscrasias such as potentially fatal agranulocytosis, and it has been associated with increased mortality compared with placebo in certain populations. In addition to acting as a sodium channel blocker, it blocks potassium channels and prolongs the QT interval, which leads to a proarrhythmic effect. It should not be used in clients with certain heart blocks or in those with systemic lupus erythematosus or torsade de pointes. Procainamide can cause hypotension, so the nurse must be mindful of maximum infusion rates to minimize this possibility. The nurse will also need to monitor the client's ECG, CBC, and drug levels of procainamide and its active metabolite, N-acetyl procainamide.

Lidocaine can cause central nervous system toxicity. The nurse will need to monitor the client's ECG continuously and may need to monitor the client's blood levels for the drug, depending on how long it will be administered.

Flecainide carries a warning because it can cause 1:1 AV conduction in atrial fibrillation/flutter. This means that the ventricles will beat once for each impulse in the atria, which is so fast that it can cause hemodynamic collapse. The nurse should monitor the client's ECG and any blood levels ordered.

Contraindications vary based on the drug. Some of the most noteworthy contraindications include:

- Quinidine and procainamide should not be used in clients with baseline prolonged QT interval, given their effect on the QT interval. They also should not be used with other drugs that strongly prolong the QT interval. Procainamide is contraindicated in clients who have systemic lupus erythematosus.
- Lidocaine is contraindicated in individuals with an arrhythmia called Wolff–Parkinson–White syndrome and in those with certain heart blocks.
- Flecainide and propafenone are contraindicated in clients with structural heart disease, such as heart failure or myocardial infarction, due to potentially fatal proarrhythmic effects and worsening of heart failure.

Table 17.3 is a drug prototype table for sodium channel blockers featuring the class IB drug lidocaine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Sodium channel blocker **Mechanism of Action** Blocks sodium channels in the cells of the cardiac conduction system	**Drug Dosage** *Ventricular arrhythmias (hemodynamically stable):* 1–1.5 mg/kg IV bolus, repeat 0.5–0.75 mg/kg IV bolus every 5–10 minutes; maintenance infusion is 1–4 mg/minute IV.
Indications Acute treatment of ventricular cardiac arrhythmias Local and regional anesthesia **Therapeutic Effects** Facilitates cardioversion Maintains normal sinus rhythm	**Drug Interactions** Digoxin (toxicity) Beta-adrenergic blockers **Food Interactions** No significant interactions
Adverse Effects Bradycardia Hemodynamic collapse Atrioventricular block Sinus arrest Delirium Psychosis Seizure Nausea Tinnitus Dyspnea Bronchospasm	**Contraindications** Hypersensitivity Severe sinoatrial node disfunction, aortic stenosis, or intraventricular blocks

TABLE 17.3 **Drug Prototype Table: Lidocaine** (sources: https://dailymed.nlm.nih.gov/dailymed/; Al-Khatib et al., 2018)

Nursing Implications

The nurse should do the following for clients who are taking sodium channel blockers:

- Recognize and monitor for serious and potentially dangerous adverse effects of these drugs.
- Monitor the ECG of any client who takes antiarrhythmic drugs, paying careful attention to the QT interval.
- Monitor blood levels of drugs and relevant metabolites.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking *quinidine* should:

- Report excessive diarrhea to their health care provider.

The client taking *mexiletine* should:

- Report signs and symptoms of hepatic toxicity, such as jaundice.

The client taking *propafenone* should:

- Report signs of infection due to agranulocytosis, such as fever or sore throat.

FDA BLACK BOX WARNING

Quinidine

Active antiarrhythmic therapy has resulted in increased mortality; the risk of active therapy is greatest in clients with structural heart disease.

Procainamide

Prolonged administration of procainamide often leads to the development of a positive antinuclear antibody test, with or without symptoms of lupus erythematosus–like syndrome. If a positive antinuclear antibody titer develops, the benefits versus the risks of continued procainamide therapy should be assessed. In addition, agranulocytosis, bone marrow depression, neutropenia, hypoplastic anemia, and thrombocytopenia in clients receiving procainamide HCl have been reported at a rate of approximately 0.5%.

Mexiletine

In postmarketing experience, abnormal liver function tests have been reported, some in the first few weeks of therapy.

Flecainide

A review of the world literature revealed reports of ventricular tachycardia in 0.4% of clients receiving flecainide. Of 19 clients reported in the literature with chronic atrial fibrillation, 10.5% experienced ventricular tachycardia or ventricular fibrillation. Flecainide is not recommended for use in clients with chronic atrial fibrillation.

Flecainide, Propafenone, Mexiletine, Procainamide

In the CAST trial, there was excessive mortality in post–myocardial infarction clients who were administered flecainide or another similar drug, encainide.

17.3 Class II: Beta Adrenergic Blockers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 17.3.1 Identify the characteristics of the beta-adrenergic blocker drugs used to treat dysrhythmias.
- 17.3.2 Explain the indications, actions, adverse reactions, and interactions of beta-adrenergic blocker drugs used to treat dysrhythmias.
- 17.3.3 Describe the nursing implications of beta-adrenergic blocker drugs used to treat dysrhythmias.
- 17.3.4 Explain the client education related to beta-adrenergic blocker drugs used to treat dysrhythmias.

Beta-adrenergic blockers (informally called *beta blockers*) are known by their generic names, which end with "olol." They can be used for many disease states, including heart failure, myocardial infarction, angina, and hypertension. Beta-adrenergic blockers block adrenergic beta-1 receptors in the heart (among other actions, depending on the drug), which leads to decreased heart rate from the SA node. It also leads to a decreased rate of conduction through the AV node and decreased cardiac contractility. There are other types of beta-adrenergic receptors, such as beta-2 receptors in the lungs that mediate bronchoconstriction. Some beta-adrenergic blockers can also affect alpha receptors in the vasculature, causing vasodilation and decreased blood pressure. Many beta-adrenergic blockers are used in practice; however, it is most common to use the ones that are cardioselective for treatment of arrhythmias. Clients should avoid stopping beta-adrenergic blockers abruptly because sudden discontinuation can exacerbate arrhythmias.

SAFETY ALERT

Beta-Adrenergic Blockers

Beta-adrenergic blockers can cause bradycardia. The nurse should monitor the client's heart rate before administration and not give the drug to bradycardic clients who do not have a functioning pacemaker.

Many beta-adrenergic blockers are available, and several can be used as antidysrhythmic drugs. This chapter discusses two of the most common beta-adrenergic blockers: esmolol and metoprolol.

Esmolol

Esmolol is an intravenous beta-adrenergic blocker that is selective for the beta-1 receptors in the heart. Esmolol is very fast acting and slows the heart rate within 2–10 min of administration. It also has a short duration; the half-life of esmolol in adults is only 9 min. For this reason, esmolol is often administered as a short-term treatment (used less than 48 hours) via continuous infusion when acute control is needed or for ease of titration. It is approved for sinus tachycardia, supraventricular tachycardia, atrial fibrillation/flutter, and intraoperative and postoperative tachycardia and hypertension. It is used off-label for ventricular tachycardia. Frequent blood pressure monitoring is required. An arterial line provides the best method for continuous monitoring of blood pressure, although it is an invasive procedure and not always done (Pevtsov & Fredlund, 2023).

CLINICAL TIP

Administration of Esmolol

Esmolol is a vesicant, and extravasation can lead to skin necrosis and sloughing. The nurse should ensure proper needle/catheter placement. If extravasation occurs, the infusion should be stopped, the line aspirated, and the limb elevated.

Metoprolol

Metoprolol is a beta-adrenergic blocker with selective activity at beta-1 receptors in the heart. It is available as an immediate-release tablet (metoprolol tartrate) and an extended-release tablet (metoprolol succinate). It is also available in an intravenous form. It is approved for various cardiac conditions, including heart failure, angina, hypertension, and myocardial infarction. It is used off-label for treating atrial fibrillation/flutter, other supraventricular arrhythmias, and ventricular arrhythmias.

Table 17.4 lists common cardioselective beta-adrenergic blockers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Esmolol (Brevibloc)	*Rate control of atrial fibrillation:* 500 mcg/kg IV bolus over 1 minute, then 50–300 mcg/kg/minute IV.
Metoprolol (Lopressor, Toprol XL)	*Rate control of atrial fibrillation:* *Metoprolol tartrate (immediate release):* *IV:* 2.5–5 mg IV over 2 minutes, up to 3 doses. *Oral:* 25–100 mg orally twice daily. *Metoprolol succinate (extended release):* 50–400 mg orally daily.
Atenolol (Tenormin)	*Rate control of atrial fibrillation:* 25–100 mg orally daily.
Propranolol (Inderal)	*Rate control of atrial fibrillation:* *IV:* 1 mg IV over 1 minute, up to 3 doses at 2-minute intervals. *Oral:* 10–40 mg orally 3–4 times daily.
Bisoprolol	*Rate control of atrial fibrillation:* 2.5–10 mg orally daily.

TABLE 17.4 Drug Emphasis Table: Beta-Adrenergic Blockers (sources: https://dailymed.nlm.nih.gov/dailymed/; January et al., 2014)

Adverse Effects and Contraindications

Cardioselective beta-adrenergic blockers do not have direct hypotensive effects on the vasculature but can still cause hypotension through decreased cardiac output. Beta-adrenergic blockers can mask hypoglycemia due to their effects on heart rate, so clients with diabetes should be aware that they will not necessarily experience their typical hypoglycemic symptoms. Beta-adrenergic blockers can cause central nervous system adverse effects, especially fatigue. They also can be associated with bronchospasm; however, cardioselective beta-adrenergic blockers have a lower risk for this. Sexual side effects are also common.

Although beta-adrenergic blockers are indicated to treat heart failure long term, starting beta-adrenergic blockers too quickly or at too high a dose can lead to heart failure exacerbations because of their effect on cardiac

contractility.

Beta-adrenergic blockers can cause bradycardia and are contraindicated in clients who have severe bradycardia unless they have a pacemaker and in clients in cardiogenic shock. They should also be used cautiously in clients with acute exacerbations of heart failure.

Table 17.5 is a drug prototype table for beta-adrenergic blockers featuring metoprolol. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Beta-adrenergic blocker **Mechanism of Action** Acts as a beta-1 receptor antagonist in cardiac tissue, slowing pacing from the sinoatrial node and conduction through the atrioventricular node	**Drug Dosage** *Rate control of atrial fibrillation:* *Metoprolol tartrate (immediate release):* *IV:* 2.5–5 mg IV over 2 minutes, up to 3 doses. *Oral:* 25–100 mg orally twice daily. *Metoprolol succinate (extended release):* 50–400 mg orally daily.
Indications Rate control of atrial fibrillation/flutter Angina Heart failure Hypertension Myocardial infarction **Therapeutic Effects** Decreases heart rate and conduction Decreases cardiac contractility (not related to antiarrhythmic effects)	**Drug Interactions** Reserpine Digoxin Calcium channel blockers CYP2D6 inhibitors Alpha-adrenergic blockers Ergot alkaloids **Food Interactions** No significant interactions
Adverse Effects Fatigue Dizziness Bradycardia Bronchospasm Hypotension Heart failure Heart blocks	**Contraindications** Sinus bradycardia Heart blocks Cardiogenic shock Overt cardiac failure Sick sinus syndrome Severe peripheral arterial circulatory disorders Acute myocardial infarction, especially with hemodynamic instability Hypotension (systolic blood pressure less than 100 mm Hg) Caution: Bronchospastic disease

TABLE 17.5 **Drug Prototype Table: Metoprolol** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking beta-adrenergic blockers:

- If the baseline heart rate is less than 60 beats per minute, consider checking with the health care provider before giving the drug.
- Monitor the client's blood pressure.
- Recognize differences in dosing regimens between IV and oral forms of the drugs.
- Take care to avoid and recognize extravasation of esmolol.
- Be careful not to confuse the different forms of metoprolol.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a beta-adrenergic blocker should:

- Avoid orthostatic hypotension by moving slowly when standing up from a sitting or lying position. Extra caution is advised after dose increases.
- *Not* stop their medication abruptly because this can cause arrhythmias and produce withdrawal effects.
- Alert their health care provider if they feel very dizzy.
- Understand that beta-adrenergic blockers can worsen respiratory symptoms of asthma and chronic obstructive pulmonary disease (COPD).
- Be aware that beta-adrenergic blockers can mask symptoms of hypoglycemia. (This is particularly important for clients with diabetes.)

FDA BLACK BOX WARNING

Beta-Adrenergic Blockers

Metoprolol: Following abrupt cessation of therapy with certain beta-blocking agents, myocardial infarction and exacerbations of angina pectoris have occurred.

Atenolol: Advise clients with coronary artery disease who are being treated with atenolol against abruptly stopping the medication. Severe exacerbation of angina and the occurrence of myocardial infarction and ventricular arrhythmias have been reported in clients with angina following the abrupt discontinuation of therapy with beta-adrenergic blockers.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Mike Smith is a 73-year-old client who presents to the emergency department with symptoms of a racing heart. The nurse checks his ECG and notices no discernable P waves and narrow QRS (ventricular depolarization) complexes.

History
This client has a past medical history of type 2 diabetes and hypercholesterolemia.

Current Medications
Omeprazole 20 mg daily

Vital Signs		Physical Examination
Temperature:	98.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; no peripheral edema noted; S1, S2 noted, irregularly regular heart rhythm • *Respiratory:* Within normal limits • *Gastrointestinal:* Abdomen soft, nontender, nondistended • *Genitourinary:* Reports normal urine output • *Neurological:* Within normal limits • *Integumentary:* No wounds noted; skin appropriate for age
Blood pressure:	100/72 mm Hg	
Heart rate:	132 beats/min	
Respiratory rate:	17 breaths/min	
Oxygen saturation:	99% on room air	
Height:	5'10"	

TABLE 17.6

Vital Signs		Physical Examination
Weight:	202 lb	

TABLE 17.6

1. Based on the information above, the nurse anticipates which diagnosis by the health care provider?
   a. Ventricular fibrillation
   b. Ventricular tachycardia
   c. Atrial fibrillation with rapid ventricular response
   d. Torsade de pointes

2. Which medication may be given to treat the client's diagnosis?
   a. Procainamide
   b. Mexiletine
   c. Lidocaine
   d. Metoprolol

17.4 Class III: Potassium Channel Blockers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 17.4.1 Identify the characteristics of the potassium channel blocker drugs used to treat dysrhythmias.
- 17.4.2 Explain the indications, actions, adverse reactions, and interactions of potassium channel blocker drugs used to treat dysrhythmias.
- 17.4.3 Describe the nursing implications of potassium channel blocker drugs used to treat dysrhythmias.
- 17.4.4 Explain the client education related to potassium channel blocker drugs used to treat dysrhythmias.

Potassium channel blockers are class III drugs. They work by blocking the potassium channels that facilitate potassium transport and mediate repolarization of the cardiac cells. They extend the action potential and slow repolarization. All antidysrhythmic drugs that block potassium channels are proarrhythmic. They lead to a prolonged QT interval, which increases the risk for torsade de pointes. Because of this, all drugs within this class require ECG monitoring for QT interval assessment. The nurse must also be vigilant to consider concomitant drugs that increase the QT interval because concomitant use can have additive effects. Although all drugs within this class block potassium channels, many have additional antidysrhythmic mechanisms.

CLINICAL TIP

Monitor Potassium Channel Blockers Using the Corrected QT Interval

The QT interval changes depending on the client's heart rate. To standardize assessment, the QT interval can be corrected (adjusted) for heart rate using various methods. This correction is referred to as the QTc and is usually used in drug titration and safety algorithms. The most common formula for QTc is known as the Bazett formula. Various websites have QTc calculators (https://openstax.org/r/mayoclinicorga), and some ECG software calculates the QTc automatically.

The following medications are all classified as potassium channel blockers; however, it is important to note their additional mechanisms of action as well.

Amiodarone and Dronedarone

Amiodarone is a class III antidysrhythmic drug; however, it has all four Vaughan Williams mechanisms: It blocks sodium channels (class I), functions as a beta-adrenergic blocker (class II), blocks potassium channels (class III), and blocks calcium channels (class IV). It is available in both intravenous and oral dosage forms. Amiodarone is known for having a very long half-life (greater than 1 month); thus, the duration of action can be several months after chronic therapy ends. The nurse should be aware that even after amiodarone administration is discontinued,

its effects will be apparent for several weeks to months.

Amiodarone has many notable drug interactions. When metabolism occurs in the liver, it does so by the hepatic microsomal enzyme system. A key component of this system is an enzyme complex known as cytochrome P450 or CYP450. This enzyme metabolizes drugs, nutrients, and other substances such as steroids and cholesterol. CYP3A, CYP2C8, and others are isoenzymes of CYP450 and perform slightly different metabolic functions. The thing to remember is that these enzymes determine the speed of the metabolism of drugs and affect many drug-drug interactions. Amiodarone is a substrate for CYP3A and CYP2C8, so inducers and inhibitors of those enzymes affect the client's exposure to amiodarone. Amiodarone is also an inhibitor of P-glycoprotein and CYP1A2, CYP2C9, CYP2D6, and CYP3A; this can increase the client's exposure to other drugs that are substrates of those enzymes. Some drug interactions include:

- *Digoxin:* Amiodarone can increase digoxin concentrations. Therefore, it is recommended that digoxin doses be decreased (with careful monitoring) or discontinued altogether if amiodarone is initiated.
- *Warfarin:* Concomitant administration of warfarin and amiodarone increases the anticoagulant effect of warfarin. It is recommended to decrease the warfarin dose by one-third to one-half and to monitor prothrombin time.
- *Statin medications:* Concomitant administration of certain statin medications with amiodarone can result in increased concentrations of the statin drug. Lower starting doses of statin medications may be required; the maximum recommended dose for lovastatin is 40 mg and for simvastatin is 20 mg during concomitant use with amiodarone.

Dronedarone is like amiodarone in that it is categorized as a class III drug with all four Vaughan Williams mechanisms of action. It is approved to treat clients with paroxysmal or persistent atrial fibrillation. Because of the potential for teratogenicity, dronedarone is also classified as a hazardous drug; nurses should wear gloves when handling or administering it and follow institutional policies for hazardous drugs (Institute for Safe Medication Practices, 2018).

Dronedarone interacts with many drugs because it is an inhibitor of CYP3A and CYP2D6. Medications it interacts with include digoxin, calcium channel blockers, and statins.

Dofetilide and Ibutilide

Dofetilide and ibutilide are both pure class III antidysrhythmic medications with no additional mechanisms of action. Dofetilide is an oral medication used for atrial fibrillation and atrial flutter. It has a high risk for causing proarrhythmia, specifically torsade de pointes. Therefore, dofetilide must be initiated in a health care setting capable of providing cardiac resuscitation services and continuous ECG monitoring for a minimum of 3 days. The manufacturer's labeling provides detailed guidance for dosing and monitoring. Dofetilide is contraindicated in clients with a baseline QTc greater than 440 msec, and the drug should either be dose-adjusted or discontinued if the QTc rises above 500 msec during therapy, depending on the circumstance. Before starting dofetilide, clients should have electrolyte levels checked (potassium, magnesium), and electrolyte supplements should be administered to maintain adequate levels. Renal function must also be monitored because dofetilide is excreted by the kidneys.

Ibutilide is an intravenous class III antidysrhythmic medication. It is used almost exclusively for conversion of recent-onset atrial fibrillation or atrial flutter to sinus rhythm and given as only one or two doses (no chronic maintenance dosing). Ibutilide has a high risk for causing torsade de pointes (1.7% in registry studies; DailyMed *Ibutilide fumarate*, 2020) and should be prescribed by health care providers who are familiar with identifying and treating acute ventricular arrhythmias. It requires continuous ECG monitoring and observation for at least 4 hours after administration. Clients with atrial fibrillation for more than 2–3 days require anticoagulation for 2 weeks before administration to mitigate the risk for stroke upon cardioversion. Clients with chronic atrial fibrillation are not candidates for cardioversion using ibutilide because it is less effective than in paroxysmal (i.e., intermittent) atrial fibrillation and is associated with high risks.

Sotalol

Sotalol is another class III antidysrhythmic drug; however, in addition to its mechanism as a potassium channel blocker, it also has beta-adrenergic blocking effects. (Note that the name ends in "lol" like other beta-adrenergic

blockers.) Sotalol is available in both oral and intravenous dosage forms and is approved for the treatment of symptomatic atrial fibrillation/flutter and life-threatening ventricular arrhythmias.

As with all potassium channel blockers, sotalol prolongs the QTc interval and can cause torsade de pointes. Therefore, sotalol requires inpatient initiation in a facility that can provide cardiac resuscitation services and continuous ECG monitoring. If the client's baseline QTc interval is longer than 450 msec, sotalol should not be initiated. The manufacturer's labeling provides detailed directions for initiation and monitoring. During initiation, the client's ECG is monitored after every dose; once stable, it is monitored periodically for the duration of therapy. If the QTc interval increases to more than 500 msec during therapy, the dosing interval must be lengthened or the drug discontinued.

Sotalol is eliminated via the kidneys; thus, clients with severe renal dysfunction should not take sotalol, and renal function should be monitored periodically in all clients who take sotalol.

Table 17.7 lists common potassium channel blockers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Amiodarone (Nexterone, Pacerone)	*Ventricular dysrhythmias:* *Oral:* 800–1600 mg daily until therapeutic response occurs (usually 1–3 weeks), then reduce to 600–800 mg daily for 1 month, then 400 mg orally once daily. *IV:* For the first 24 hours, administer 150 mg IV over the first 10 minutes, followed by 360 mg IV over the next 6 hours, followed by 540 mg IV over the remaining 18 hours. After the first 24 hours, continue the maintenance infusion rate of 0.5 mg/min.
Dronedarone (Multaq)	*Atrial fibrillation:* 400 mg orally twice daily.
Dofetilide (Tikosyn)	*Atrial fibrillation:* 500 mcg orally every 12 hours; precise dosing is required, with doses spaced 12 hours apart.
Ibutilide (Corvert)	*Atrial fibrillation/atrial flutter:* 1 mg IV once. If dysrhythmia has not stopped by 10 minutes after completion of administration, a second dose may be given (dosing applies to clients who weigh at least 60 kg).
Sotalol (Betapace, Betapace AF, Sorine)	*Ventricular dysrhythmias:* 160 mg orally twice daily. *Atrial fibrillation/atrial flutter:* 80–120 mg orally twice daily.

TABLE 17.7 Drug Emphasis Table: Potassium Channel Blockers (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

All class III drugs are proarrhythmic and can cause QT prolongation, leading to torsade de pointes. Aside from that, the adverse effect profile depends on the agent being used.

Amiodarone has many potential toxicities and adverse effects, which include:

- Optic neuropathy and/or optic neuritis, which can lead to permanent blindness; corneal microdeposits that may be reversible
- Photosensitivity resulting in a bluish-gray discoloration of the skin
- New arrhythmias, including torsade de pointes
- Hyperthyroidism or hypothyroidism
- Hepatotoxicity
- Acute and chronic pulmonary toxicity, including acute respiratory distress syndrome and pulmonary fibrosis

Because of these toxicities, amiodarone requires baseline monitoring as well as follow-up monitoring at least every 3–6 months. Clients should minimally receive the following tests at baseline and periodically after initiation:

- Cardiac monitoring, including an ECG to assess heart rate, medication efficacy, and the QT interval
- Pulmonary function tests and a chest x-ray
- Liver function tests

- Thyroid function tests
- Ophthalmic exams

As with all beta-adrenergic blockers and calcium channel blockers, amiodarone can cause bradycardia, hypotension, and fatigue. Amiodarone carries multiple boxed warnings from the FDA related to arrhythmias, pulmonary toxicity, and hepatotoxicity. It is on the Beers Criteria® list of high-risk medications for older adults because of its potential for toxicity (American Geriatrics Society, 2019). Amiodarone should not be used in clients with bradycardia at baseline unless they have a pacemaker. Amiodarone has iodine within its chemical structure; thus, it is contraindicated in clients with iodine hypersensitivity.

Dronedarone has many of the same adverse effects as amiodarone, including heart failure, hepatotoxicity, QT prolongation/torsade de pointes, and pulmonary toxicity. Because of a particularly high risk for adverse reactions, including death, it is contraindicated in clients with heart failure and those in atrial fibrillation who cannot be converted to sinus rhythm; these contraindications are listed as boxed warnings from the FDA. Dronedarone is contraindicated in pregnant clients due to the potential for teratogenicity.

Dofetilide and sotalol are contraindicated in clients with severe kidney disease.

Sotalol, like all beta-adrenergic blockers, can cause bradycardia, hypotension, and fatigue and should be used cautiously in clients with asthma and heart failure.

Table 17.8 is a drug prototype table for potassium channel blockers featuring dofetilide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Potassium channel blocker antidysrhythmic **Mechanism of Action** Blocks the potassium channels responsible for repolarization of the cell, leading to a prolonged action potential and prolonged refractoriness	**Drug Dosage** *Atrial fibrillation/atrial flutter:* 500 mcg orally every 12 hours; precise dosing is required, with doses spaced 12 hours apart.
Indications Atrial fibrillation and atrial flutter **Therapeutic Effects** Converts atrial fibrillation to sinus rhythm Maintains sinus rhythm after cardioversion	**Drug Interactions** Cimetidine Trimethoprim Ketoconazole Prochlorperazine Dolutegravir Megestrol Potassium-depleting diuretics (e.g., hydrochlorothiazide) Drugs that prolong the QT interval **Food Interactions** No significant interactions
Adverse Effects QT prolongation Torsade de pointes Chest pain Headache	**Contraindications** Hypersensitivity Baseline QTc greater than 440 msec Severe renal impairment (creatinine clearance less than 20 mL/min) Caution: Renal impairment

TABLE 17.8 **Drug Prototype Table: Dofetilide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking potassium channel blockers:

- Perform a complete medication history to assess for relevant drug interactions, including other drugs that also prolong the QTc interval.
- Monitor ECG (including QTc interval), vital signs, and electrolyte levels.
- Be prepared to perform cardiac resuscitation on any client starting on a class III antidysrhythmic drug.
- Follow the specific dosing and monitoring protocols described in the manufacturer's labeling for a client initiating sotalol or dofetilide.
- Observe the client closely for at least 4 hours after administration of ibutilide for maintenance of sinus rhythm and adverse effects such as ventricular arrhythmias.
- Conduct in-depth education for any client being started on amiodarone.
- Monitor for amiodarone-related toxicity in any client taking the drug and for several months after amiodarone discontinuation.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a potassium channel blocker should:

- Communicate their baseline medication list and any new medications (such as antibiotics) to their prescribing health care provider.
- Seek emergency medical attention if they experience symptoms of torsade de pointes (dizziness, palpitations, lightheadedness, syncope).
- Keep appointments for laboratory testing to monitor for potential toxicities.

The client taking amiodarone should:

- Avoid direct sunlight and wear sunscreen and protective clothing.
- Report symptoms of hyperthyroidism (heat sensitivity, anxiety, weight loss) or hypothyroidism (fatigue, weight gain, cold sensitivity).
- Report any vision changes or breathing difficulties.
- Avoid eating grapefruits or drinking grapefruit juice.

FDA BLACK BOX WARNING

Amiodarone

Amiodarone can cause pulmonary toxicity (hypersensitivity pneumonitis or interstitial/alveolar pneumonitis) that has resulted in clinically manifest disease at rates as high as 17% in some series of clients. Pulmonary toxicity has been fatal about 10% of the time. The client should have a baseline chest x-ray and pulmonary function tests, including diffusion capacity, when amiodarone therapy is initiated. The medical history, physical exam, and chest x-ray should be repeated every 3–6 months.

Amiodarone also can cause hepatotoxicity, which can be fatal. Baseline and periodic liver transaminase levels should be obtained, and the medication should be discontinued or reduced in dose if the level exceeds three times the normal level or doubles in a client with an elevated baseline. Amiodarone should be stopped if the client experiences signs or symptoms of clinical liver injury.

Amiodarone is intended for use only in clients with indicated life-threatening arrhythmias because its use is accompanied by substantial toxicity.

In addition, amiodarone can exacerbate arrhythmias. Amiodarone must be initiated in a clinical setting where continuous ECG monitoring and cardiac resuscitation are available.

Dronedarone

Dronedarone is contraindicated in clients with symptomatic heart failure with recent decompensation requiring

hospitalization or in clients with New York Heart Association class IV heart failure. Dronedarone doubles the risk of death in these clients. Dronedarone is contraindicated in clients in atrial fibrillation who will not or cannot be cardioverted into normal sinus rhythm. In clients with permanent atrial fibrillation, dronedarone doubles the risk of death, stroke, and hospitalization for heart failure.

Dofetilide

To minimize the risk for induced arrhythmia, clients initiated or reinitiated on dofetilide should be admitted for a minimum of 3 days into a facility that can provide calculations of creatinine clearance, continuous ECG monitoring, and cardiac resuscitation.

Sotalol

To minimize the risk of drug-induced arrhythmia, clients should be initiated, reinitiated, or up-titrated in a facility that can provide cardiac resuscitation and continuous ECG monitoring. Sotalol can cause life-threatening ventricular tachycardia associated with QT interval prolongation. A client whose baseline QTc is longer than 450 msec should not start sotalol therapy. If the QT interval lengthens to 500 msec or more, the dose should be reduced, the dosing interval lengthened, or the drug discontinued. The creatinine clearance should be calculated to determine appropriate dosing.

17.5 Class IV: Calcium Channel Blockers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 17.5.1 Identify the characteristics of the calcium channel blocker drugs used to treat dysrhythmias.
- 17.5.2 Explain the indications, actions, adverse reactions, and interactions of calcium channel blocker drugs used to treat dysrhythmias.
- 17.5.3 Describe the nursing implications of calcium channel blocker drugs used to treat dysrhythmias.
- 17.5.4 Explain the client education related to calcium channel blocker drugs used to treat dysrhythmias.

Calcium has several roles within cardiac tissue. It flows into the cells of the SA node (the pacemaker of the heart) and AV node to mediate the heart rate and conduct electrical signals from the atria to the ventricles. Calcium also facilitates contraction of the cardiac myocytes when stimulated by the cardiac conduction system. Outside the heart, calcium facilitates arterial vasoconstriction, which in turn maintains blood pressure.

Antidysrhythmic calcium channel blockers are class IV Vaughan Williams drugs and are also known as nondihydropyridine (non-DHP) calcium channel blockers. They inhibit calcium channels in cardiac cells, resulting in a slower heart rate, slower conduction through the AV node, and a decreased force of contraction. Calcium channel blockers are useful for slowing the heart rate in clients with atrial fibrillation with rapid ventricular response because they slow down the conduction of abnormal impulses through the AV node, thus decreasing the rate at which the ventricles are prompted to contract.

Many calcium channel blockers have drug interactions, which warrant vigilant assessment. Specific drug interactions will be discussed for the agents in the following sections.

SAFETY ALERT

Calcium Channel Blockers

Calcium channel blocker antidysrhythmic drugs reduce heart rate and blood pressure. The nurse must monitor the baseline heart rate and blood pressure before administering a calcium channel blocker and then monitor them frequently during therapy. If the baseline heart rate is less than 60 beats per minute, consider checking with the health care provider before administration.

Another class of calcium channel blockers, the DHP calcium channel blockers, block calcium channels only within arteries, not within the heart. Therefore, DHP calcium channel blockers are useful for treating hypertension but not for treating dysrhythmias. See Antihypertensive and Antianginal Drugs for more information about hypertension

treatment.

The most common non-DHP calcium channel blockers are diltiazem and verapamil.

Diltiazem

Diltiazem is a non-DHP calcium channel blocker antidysrhythmic. It is available in both oral and intravenous dosage forms; oral options include immediate-release and extended-release products. It is FDA approved for hypertension and angina. The intravenous form is also FDA approved for heart rate control in atrial fibrillation. Although oral diltiazem is not FDA approved for this condition, national guidelines do recommend its use for this indication (January et al., 2014).

Many different companies manufacture oral diltiazem as similar but not bioequivalent generic products, which can lead to confusion during prescribing and administration. Some examples are Cardizem, Cartia XT, Dilt-XR, Taztia XT, Tiadylt ER, and Matzim LA. The nurse should take an accurate medication history with the specific medication the client takes and be careful to avoid confusing the various products.

Diltiazem has a notable drug interaction with simvastatin. The FDA recommends limiting the dose of simvastatin to 10 mg daily with concomitant use because it can result in increased plasma levels of simvastatin, leading to adverse events (Hopewell et al., 2020; U.S. Food and Drug Administration, 2017).

Verapamil

Verapamil is a non-DHP calcium channel blocker approved for the treatment of angina, atrial fibrillation/atrial flutter, hypertension, and supraventricular tachycardia. It is available in both oral and intravenous dosage forms. As with diltiazem, the FDA recommends limiting the dose of simvastatin to 10 mg daily with concomitant use because it can result in increased plasma levels of simvastatin, leading to adverse events (Hopewell et al., 2020; U.S. Food and Drug Administration, 2017).

Table 17.9 lists common calcium channel blockers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Diltiazem (Cardizem, Cartia XT, Dilt XR, Taztia XT, Tiazac)	*Atrial fibrillation:* *Extended-release:* 120–360 mg orally daily. IV: 0.25 mg/kg IV bolus over 2 minutes, then 5–15 mg/hour continuous IV infusion.
Verapamil (Calan SR)	*Atrial fibrillation:* 0.075–0.15 mg/kg IV bolus over 2 minutes, then 0.005 mg/kg/min continuous IV infusion.

TABLE 17.9 Drug Emphasis Table: Calcium Channel Blockers (source: https://dailymed.nlm.nih.gov/dailymed/; January et al., 2014)

Adverse Effects and Contraindications

Calcium channel blockers can cause bradycardia as an extension of their therapeutic effect. They also decrease arterial vasoconstriction, which reduces blood pressure and can cause hypotension. Additionally, they can cause swelling and edema.

Because calcium is important for facilitating ventricular contraction, calcium channel blockers can decrease contractility of the heart. This can be particularly troublesome in clients with heart failure with reduced ejection fraction or acute myocardial infarction, who already have decreased contractility. For this reason, non-DHP calcium channel blockers should be used cautiously or avoided in those clients. They should also be avoided in clients who have bradycardia or AV blocks without a pacemaker or those receiving beta-adrenergic blockers.

Table 17.10 is a drug prototype table for calcium channel blockers featuring diltiazem. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nondihydropyridine calcium channel blocker **Mechanism of Action** Inhibits the calcium channel in cardiac tissue and blood vessels, leading to decreased conduction through the atrioventricular node and vasodilation	**Drug Dosage** *Atrial fibrillation:* *Extended release:* 120–360 mg orally daily. *IV:* 0.25 mg/kg IV bolus over 2 minutes, then 5–15 mg/hour continuous IV infusion.
Indications Angina Hypertension Atrial fibrillation/flutter **Therapeutic Effects** Decreases heart rate Lowers blood pressure	**Drug Interactions** Substrates or inhibitors of CYP3A4 Beta-adrenergic blockers Benzodiazepines Anesthetics Clonidine Cyclosporine Digoxin Ivabradine Quinidine Rifampin Statins **Food Interactions** Alcohol Grapefruit juice
Adverse Effects Headache Dizziness Bradycardia Atrioventricular block Edema Asthenia Rash, including Stevens–Johnson syndrome	**Contraindications** Hypersensitivity Sick sinus syndrome (unless client has ventricular pacemaker) Hypotension Myocardial infarction Pulmonary congestion

TABLE 17.10 **Drug Prototype Table: Diltiazem** (source: https://dailymed.nlm.nih.gov/dailymed/; January et al., 2014)

Nursing Implications

The nurse should do the following for clients who are taking calcium channel blockers:

- Obtain a complete medication list to check for any drug interactions.
- Measure heart rate and blood pressure before administering a non-DHP calcium channel blocker.
- Notify the health care provider if the client has baseline bradycardia and does not have a pacemaker.
- Use continuous cardiac/hemodynamic monitoring in clients on intravenous calcium channel blockers.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a calcium channel blocker should:

- Contact their health care provider if they experience signs or symptoms of therapeutic failure, such as racing heart, lightheadedness, or fatigue (signs and symptoms of the dysrhythmia).
- Contact their health care provider if they experience signs or symptoms of adverse effects of the medication, such as dizziness or lightheadedness (which could indicate hypotension) or edema.
- Avoid drinking grapefruit juice.
- Keep an accurate and up-to-date medication list and provide it to their providers at each appointment in

order to avoid drug interactions.
- Monitor their heart rate and blood pressure as directed by their health care provider.

17.6 Unclassified Antidysrhythmics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 17.6.1 Identify the characteristics of unclassified drugs used to treat dysrhythmias.
- 17.6.2 Explain the indications, actions, adverse reactions, and interactions of unclassified drugs used to treat dysrhythmias.
- 17.6.3 Describe the nursing implications of unclassified drugs used to treat dysrhythmias.
- 17.6.4 Explain the client education related to unclassified drugs used to treat dysrhythmias.

Some antidysrhythmic drugs do not have a mechanism that fits into in the Vaughan Williams classification. These heterogeneous drugs do not have a unifying mechanism or treatment indication; they vary in their properties, and each will be discussed separately in the following sections.

Atropine

Atropine is an anticholinergic agent approved for symptomatic bradycardia, among other indications. It works as an acetylcholine receptor antagonist, thus decreasing parasympathetic or vagal regulation of the heart rate. It is important to note that heart transplant recipients lack vagal innervation, so atropine does not work to treat bradycardia in these clients.

Atropine should be administered by rapid intravenous injection. Slow administration of atropine has been associated with paradoxical bradycardia (McLendon & Preuss, 2022) and should be avoided.

Digoxin

Digoxin is an older antidysrhythmic drug that was first approved in 1954 and is used for rate control of atrial fibrillation or atrial flutter. As an antidysrhythmic drug, it works by suppressing conduction through the AV node, slowing the rate of conduction and, thus, the ventricular heart rate. It does this by enhancing vagal (parasympathetic) stimulation of the heart. It is also approved for treatment of heart failure with reduced ejection fraction. Clients with heart failure and concomitant atrial fibrillation have few treatment options because many of the antidysrhythmic drugs are contraindicated. Therefore, given its approval for both disease states, digoxin is sometimes used for these clients.

Digoxin is available in both oral and intravenous dosage forms. Because it is eliminated by the kidneys and can accumulate in individuals with decreased kidney function, nurses must monitor renal function in clients who are taking digoxin.

Digoxin serum levels can be monitored; the reference range is 0.5–2.0 ng/mL. However, serum levels greater than or equal to 1.2 ng/mL may be associated with higher rates of mortality (Lopes et al., 2018). For clients who present with toxicity and particularly high digoxin serum levels (greater than 6–10 ng/mL), an antidote called digoxin immune fab (Digibind) can be administered to bind the digoxin and facilitate excretion. Many health care providers monitor the apical heart rate before administering digoxin, withholding it if the apical heart rate is less than 60 beats per minute.

Adenosine

Adenosine is another unclassified antidysrhythmic drug that is approved for treating paroxysmal supraventricular tachycardia. It works by enhancing potassium efflux and suppressing calcium influx into the cells of the AV node, slowing its conduction and extinguishing arrhythmias that originate there. Adenosine is available in an intravenous dosage form. It has an extraordinarily short half-life—less than 10 seconds. This short half-life necessitates specific administration to ensure that the drug will reach the systemic circulation before it is metabolized: It must be given as a rapid IV bolus by the peripheral intravenous route, either administered directly into a vein or into an IV injection port as close to the client as possible. It must be immediately followed by a rapid saline flush. Using a stopcock can help facilitate quick administration.

After administration of adenosine, clients will frequently experience a brief period of asystole on the ECG while concurrently experiencing a sensation of their heart stopping. This occurs because for a short period, conduction through the AV node (and thus the stimulus for ventricular contraction) is blocked. The nurse should tell the client about this expected effect to mitigate anxiety when the effect occurs. It is short lived due to the short half-life; prolonged asystole is very rare. Still, adenosine should be given only with continuous ECG monitoring at a facility with resuscitation measures available.

Table 17.11 lists common unclassified antidysrhythmics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Atropine (AtroPen)	*Symptomatic bradycardia:* 0.5–1 mg IV (may be repeated every 3–5 minutes to a maximum dose of 3 mg).
Digoxin (Lanoxin)	*Rate control of atrial fibrillation:* Dosing is individualized based on client-specific factors (e.g., body weight, renal function, age), indication, and serum levels.
Adenosine (Adenocard)	*Paroxysmal supraventricular tachycardia:* 6 mg via rapid IV bolus; if therapeutic failure after 1–2 minutes, 12 mg should be given. This 12 mg dose may be repeated a second time if required.

TABLE 17.11 Drug Emphasis Table: Unclassified Antidysrhythmics (sources: https://dailymed.nlm.nih.gov/dailymed/; Kusumoto et al., 2019)

Adverse Effects and Contraindications

Atropine can cause anticholinergic adverse effects as an extension of its therapeutic effect. Some of the more serious adverse effects include tachycardia, acute glaucoma, pyloric obstruction, complete urinary retention in clients with benign prostatic hyperplasia, and formation of respiratory mucus plugs. Other common adverse effects include dry mouth, constipation, and blurred vision. Clients who cannot tolerate anticholinergic effects should avoid atropine. This caution includes individuals with myasthenia gravis or those with urinary retention because atropine can exacerbate their disease. Clients who have had a heart transplant should not rely on atropine to treat bradycardia because it may not have a therapeutic effect.

Digoxin should not be used in clients with baseline bradycardia or certain heart blocks because it can cause bradycardia as part of its therapeutic effect. Digoxin therapy has a propensity for toxicity, which is characterized by gastrointestinal upset, vision changes, dizziness, fatigue, and cardiovascular symptoms such as palpitations from premature ventricular contractions (Cummings & Swoboda, 2023).

Adenosine has a very short half-life, so adverse effects beyond the immediate period of administration are rare. However, immediately upon administration it is typical for clients to report skin flushing, sweating, nausea, and an impending sense of doom. It also can cause dyspnea (shortness of breath) and bronchoconstriction in susceptible individuals. Adenosine should not be administered to clients with second- or third-degree AV block or to those with bradycardia who do not have a pacemaker. Adenosine can cause AV block as an extension of its therapeutic effect.

Table 17.12 is a drug prototype table for unclassified antidysrhythmics featuring digoxin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Unclassified antidysrhythmic **Mechanism of Action** Suppresses conduction through the atrioventricular node (antidysrhythmic action)	**Drug Dosage** *Rate control of atrial fibrillation:* Dosing is individualized based on client-specific factors (e.g., body weight, renal function, age), indication, and serum levels.
Indications Rate control of atrial fibrillation/flutter Heart failure with reduced ejection fraction **Therapeutic Effects** Slows heart rate	**Drug Interactions** Potassium-sparing diuretics Calcium, especially IV Amiodarone Erythromycin Clarithromycin Succinylcholine Rifampin **Food Interactions** No significant interactions
Adverse Effects Heart block Anorexia Nausea Vomiting Diarrhea Visual disturbances (blurred or yellow vision) Confusion Mental disturbances (anxiety, depression, delirium, hallucination)	**Contraindications** Ventricular fibrillation

TABLE 17.12 **Drug Prototype Table: Digoxin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking unclassified antidysrhythmics:

- Obtain a complete medication list to check for any drug interactions.
- Measure heart rate and blood pressure before administering the medication.
- Monitor for adverse effects, including electrolyte imbalances and changes in kidney function.
- Notify the health care provider if the client has baseline bradycardia and does not have a pacemaker.
- Use continuous cardiac monitoring in clients using these drugs.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking *atropine* should:

- Report signs of anticholinergic adverse effects such as dry mouth, urinary retention, and constipation.

The client taking *adenosine* should:

- Be aware that its administration may feel frightening but that the adverse effects are short-lived.

The client taking *digoxin* should:

- Take care to avoid taking more of it than prescribed or more frequently than prescribed.
- Report any signs or symptoms of toxicity.

Chapter Summary

This chapter introduced various common arrhythmias and antidysrhythmic drugs for treating them. Drugs were discussed based on their primary mechanism as categorized by the Vaughan Williams classification: class I, sodium channel blockers; class II, beta-adrenergic blockers; class III, potassium channel blockers; class IV, calcium channel blockers; and unclassified antidysrhythmic drugs.

Key Terms

atrial fibrillation with rapid ventricular response atrial fibrillation with a heart rate greater than 100 beats per minute

bradycardia heart rate less than 60 beats per minute

cardioversion restoration of a normal heart rhythm in a client with a dysrhythmia

dysrhythmia an abnormal heart rate or rhythm; also called arrhythmia

proarrhythmia the propensity for a drug to create another, new dysrhythmia

supraventricular tachycardia a dysrhythmia that originates from a location above the ventricle

tachycardia heart rate greater than 100 beats per minute

torsade de pointes a dangerous ventricular tachycardia associated with medications that prolong the QT interval

vagal maneuver physical manipulation that can increase parasympathetic activation to treat various arrhythmias

Vaughan Williams classification system a method of classifying antidysrhythmic drugs based on their primary mechanism of action

ventricular tachycardia a dysrhythmia that originates from a location in the ventricle

Review Questions

1. A client accidentally took double their dose of metoprolol when confused about the directions. The nurse expects which of the following to occur?
   a. The client will experience tachycardia.
   b. The client will experience a long QT interval.
   c. The client will experience bradycardia.
   d. The client will experience torsade de pointes.

2. A nurse has an order to administer verapamil to a client with atrial fibrillation. The client has a past medical history of hyperlipidemia, type 2 diabetes, myasthenia gravis, and congestive heart failure. Which disease state may be exacerbated by administration of verapamil?
   a. Hyperlipidemia
   b. Myasthenia gravis
   c. Congestive heart failure
   d. Type 2 diabetes

3. A nurse is creating a monitoring protocol for drugs that require special monitoring of the QT interval. Which drug will be included?
   a. Lidocaine
   b. Procainamide
   c. Mexiletine
   d. Flecainide

4. A nurse provided education to a client who will be taking quinidine long term. Which response from the client indicates the teaching was effective?
   a. “I should start taking a laxative to prevent the most common side effect, constipation.”
   b. “Quinine is another name for quinidine and may be on my prescription bottle.”
   c. “I should drink grapefruit juice to ensure my vitamin levels are adequate.”
   d. “If I experience excessive diarrhea, I should alert my provider.”

5. Which of the following is an adverse effect of metoprolol?

a. Torsade de pointes
b. Fatigue
c. Tachycardia
d. Edema

6. Which arrhythmia is associated with potassium channel blockers?
a. Torsade de pointes
b. Sinus tachycardia
c. Supraventricular tachycardia
d. Atrioventricular block

7. A client is admitted to the emergency department with symptoms of dizziness and hypotension after returning from a beach vacation. The nurse notices a bluish-gray color to their skin. Which medication does the nurse suspect the client takes?
a. Diltiazem
b. Amiodarone
c. Flecainide
d. Dofetilide

8. A client is discussing chronic medication options to treat their atrial fibrillation with rapid ventricular response. The client prefers to avoid hospitalization overnight for initiation. Which of the following medications would be the best option?
a. Dofetilide
b. Metoprolol tartrate
c. Sotalol
d. Mexiletine

9. Which antidysrhythmic medication would increase the risk for statin-related adverse effects in a client who takes simvastatin?
a. Dofetilide
b. Metoprolol
c. Diltiazem
d. Mexiletine

10. An 85-year-old client takes digoxin for atrial fibrillation and is admitted to the hospital with acute kidney injury. What signs and symptoms does the nurse expect the client to be experiencing?
a. Stomach upset, vision changes, confusion
b. Constipation, photosensitivity, confusion
c. Vision changes, QT interval prolongation, photosensitivity
d. Hyperthyroidism, stomach upset, muscle pain

CHAPTER 18
Antihypertensive and Antianginal Drugs

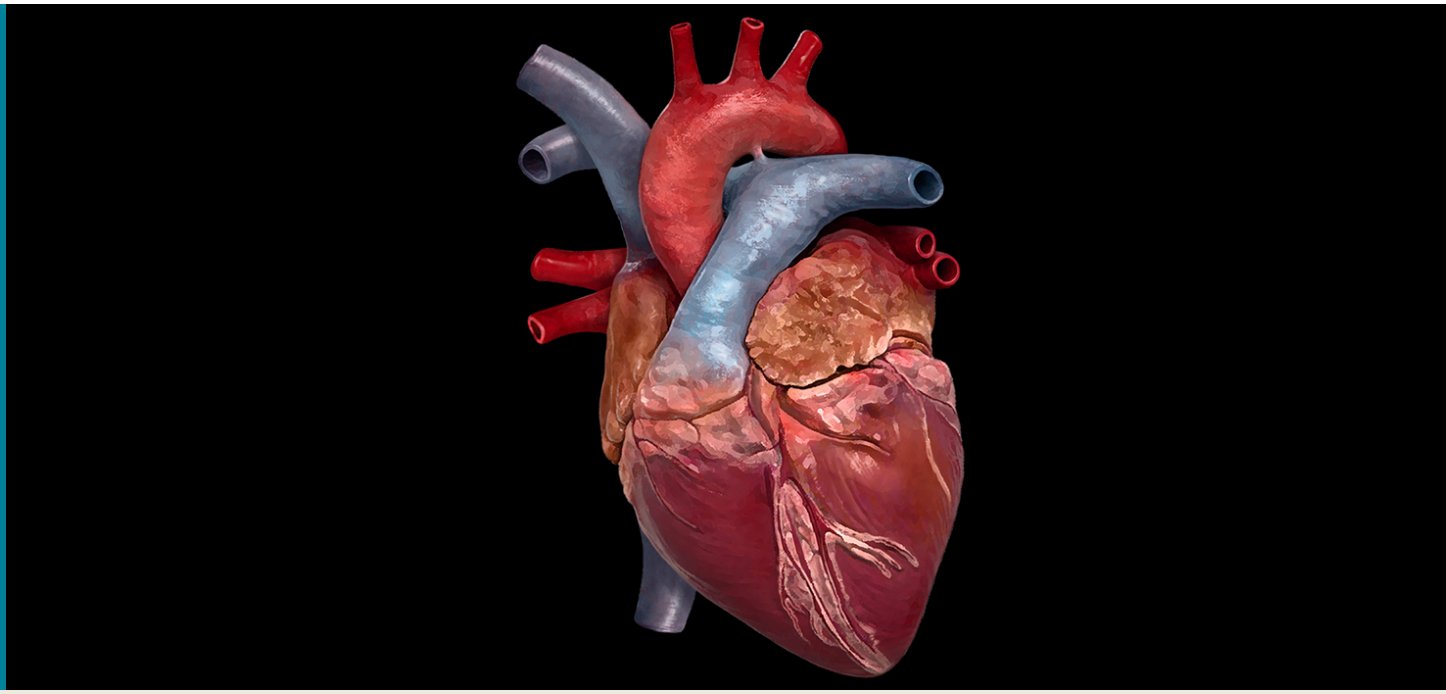


FIGURE 18.1 The heart is the primary organ of the cardiovascular system, controlling circulation and blood flow for the entire body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION **Hypertension**, a common health condition, increases a person's risk for myocardial infarction (heart attack), heart failure, renal disease, and stroke. Angina is chest pain caused by reduced blood flow to the heart. **Antihypertensive drugs** are used to treat hypertension. **Antianginal drugs**, such as nitrates and calcium channel blockers, are commonly used to treat angina. This chapter will explore hypertension and angina, and the pharmacologic and nonpharmacologic treatments for these disease processes.

18.1 Hypertension and Angina

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 18.1.1 Describe the pathophysiology of hypertension and angina.
- 18.1.2 Explain the blood pressure guidelines for determining hypertension.
- 18.1.3 Identify clinical manifestations related to hypertension and angina.
- 18.1.4 Identify etiology and diagnostic studies related to hypertension and angina.

Hypertension

The cardiovascular system transports blood and oxygen throughout the body. Blood flows from a system of higher resistance to one of lower resistance—from arteries to capillaries to veins. Blood pressure (see Figure 18.2) represents the force that blood flow exerts on arterial walls.

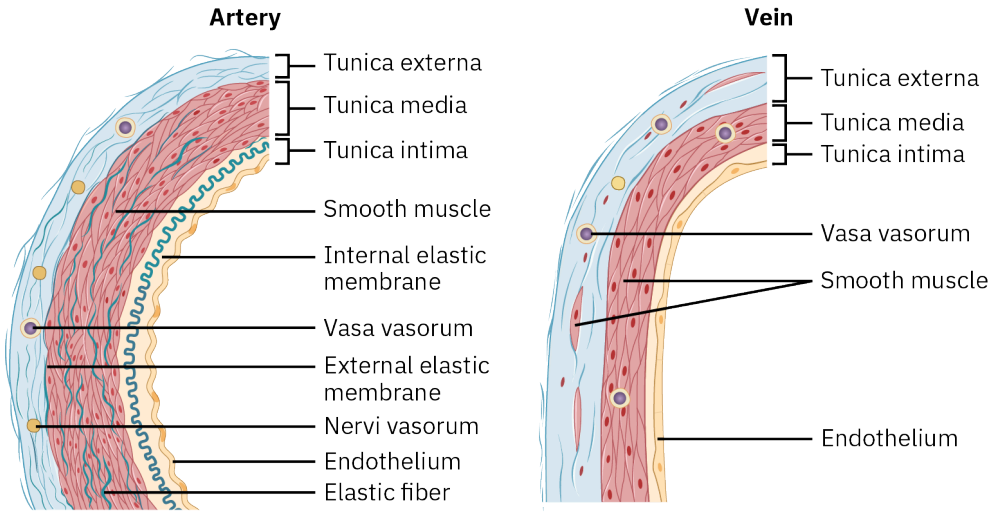


FIGURE 18.2 The walls of the arteries are much thicker than those of the veins because of the higher pressure of the blood that flows through them. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The two elements that determine blood pressure are cardiac output and peripheral vascular resistance. **Cardiac output** (CO) is the volume of blood pumped by the heart per unit of time, usually measured in liters per minute. The CO is determined by the **heart rate** (HR), the number of times the heart beats per minute, and **stroke volume** (SV)—the amount of blood ejected with each heartbeat—and is represented by the following equation:

$$\mathrm{CO} = \mathrm{HR} \times \mathrm{SV}.$$

Blood pressure is determined by examining both systolic and diastolic blood pressure readings. The **systolic blood pressure** reading represents the amount of pressure within the arteries when the heart contracts, whereas the **diastolic blood pressure** reading reflects the amount of pressure when the heart is at rest between beats. The diastolic blood pressure reading, which is the lower pressure within the arteries and vessels, determines the **peripheral vascular resistance** (also known as systemic vascular resistance) by measuring blood flow and the level of constriction or dilatation within the arteries and vessels. Blood pressure (BP) is measured in millimeters of mercury (mm Hg) and is expressed as the systolic pressure over the diastolic pressure (for instance, 125/90 mm Hg).

Hypertension occurs when an individual's blood pressure is above normal limits for a sustained period of time. Hypertension can be either primary (essential) hypertension or secondary hypertension. Primary hypertension is caused by unknown elements; however, some studies have implicated genetics and behavioral and environmental factors, including age, high salt intake, insulin resistance, obesity, high alcohol intake, sedentary lifestyle, smoking, and stress (Aggarwal et al., 2023; Iqbal & Jamal, 2022). According to the Centers for Disease Control and Prevention (n.d.), approximately 116 million adults in the United States have hypertension.

Importantly, hypertension is not limited to adults; it can also affect children and adolescents. In the United States and other countries, primary hypertension affects up to 5% of individuals in this younger age group. Developing high blood pressure during childhood can have long-term consequences, potentially leading to hypertension in adulthood and increasing the risk of heart disease, stroke, and kidney damage. Certain modifiable risk factors can be addressed for this population to improve blood pressure levels, including obesity, physical activity, and nutrition. Health care providers should always assess blood pressure in the pediatric population to promote preventive measures within families and foster healthy lifestyle habits (American Heart Association, 2023).

Secondary hypertension results from other conditions involving the central nervous system, endocrine system, and renal system and is treated along with the underlying condition. Secondary hypertension may be cured if the

treatment for the underlying condition is successful.

Hormones also impact blood pressure regulation. The **Renin-angiotensin-aldosterone system (RAAS)** and vasopressin are the main physiologic regulatory systems or pathways affecting blood pressure homeostasis. RAAS, as illustrated in Figure 18.3, is a compensatory mechanism the body activates during **hypotension** (when blood pressure is low). Renin is released from the kidneys in response to low blood pressure. Renin interacts with angiotensinogen and converts it to **angiotensin I**. The angiotensin-converting enzyme in the pulmonary blood vessel endothelium is then triggered to produce **angiotensin II**, which constricts arterioles, increasing peripheral resistance and increasing blood pressure. Angiotensin II also stimulates the adrenal medulla to produce catecholamine, which yields **aldosterone**. Aldosterone causes the kidneys to retain water and sodium, which leads to water retention and results in an increased blood volume, cardiac output, and blood pressure. **Vasopressin** is an antidiuretic hormone that regulates reabsorption of water by the kidneys; it is released by the pituitary gland in response to low blood volume. Vasopressin causes retention of body fluids, vasoconstriction, and increased blood pressure.

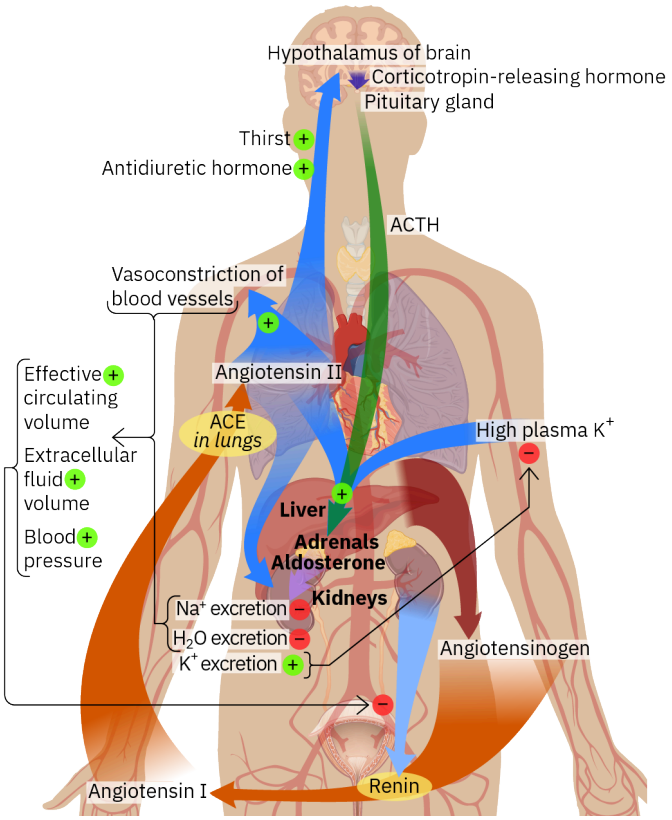


FIGURE 18.3 The renin-angiotensin-aldosterone system (RAAS) is a compensatory mechanism the body activates when blood pressure is low. (credit: modification of work "Overview of the renin-angiotensin system" by Mikael Häggström/Wikimedia Commons, Public Domain)

LINK TO LEARNING

American Heart Association and Mayo Clinic

The American Heart Association provides an interactive library on the anatomy of blood pressure (https://openstax.org/r/watchlearnlive). The library includes images and topics to explore such as the anatomy of blood pressure, high blood pressure and the cardiovascular system, and a blood pressure test.

Access multimedia content (https://openstax.org/books/pharmacology/pages/18-1-hypertension-and-angina) This video with Dr. Leslie Thomas, MD, a nephrologist at Mayo Clinic, discusses facts, questions, and answers about blood pressure to help clients better understand hypertension. The video talks about hypertension, risk factors, symptoms, diagnosis, treatment options, and coping methods to manage the disease process.

Grades of Hypertension

The American Heart Association (AHA) (n.d-a) reports that prolonged elevation of blood pressure leads to the deterioration of blood vessels. The deterioration of blood vessels is measured by grades of hypertension. Normal blood pressure is a systolic reading of less than 120 mm Hg and a diastolic reading of less than 80 mm Hg. Elevated blood pressure and hypertension increase the risk of vascular damage and decrease oxygenation. The chart below from the American College of Cardiology and AHA (see Table 18.1) demonstrates the blood pressure categories and the readings associated with them.

Blood Pressure Category	Systolic (mm Hg)		Diastolic (mm Hg)
Normal	<120	and	<80
Elevated	120–129	and	<80
Stage 1 Hypertension	130–139	or	80–89
Stage 2 Hypertension	140–180	or	90–120
Hypertensive Crisis	>180	and/or	>120

TABLE 18.1 **The American College of Cardiology and American Heart Association Categories for Hypertension** (sources: American Heart Association, https://www.heart.org/en/health-topics/high-blood-pressure/understanding-blood-pressure-readings; Centers for Disease Control and Prevention, https://www.cdc.gov/bloodpressure/facts.htm)

Diagnostics

A physical examination by a health care provider with a sphygmomanometer (blood pressure cuff or device) will identify an elevated blood pressure, and a 12-lead electrocardiogram (ECG, EKG) can assist in determining if the heart has a normal or abnormal rhythm. The health care provider also obtains blood work to determine factors that contribute to the client's hypertension as well as how the body is reacting to elevated blood pressure. These laboratory tests include a complete blood cell count (CBC), basic electrolyte panel, cholesterol panel, and renal function. An echocardiogram—an ultrasound of the heart—is not typically included in diagnostic procedures to determine hypertension; however, the health care provider may add this diagnostic study to visualize the heart's chambers, valves, and pumping action to determine the effect of hypertension on the heart, which may cause other disorders such as hypertrophy of the heart. The health care provider bases the diagnosis for hypertension on the findings of the physical examination and the diagnostic study results.

Clinical Manifestations

Symptoms of hypertension may not occur for years, and most of the time, the symptoms can be silent. Symptoms typically associated with hypertension include elevated blood pressure readings, headaches, dizziness, nausea, vomiting, visual disturbances, and neurological disturbances such as disorientation or a decreased level of consciousness. Over time, uncontrolled hypertension can lead to organ damage. Clients can experience symptoms related to the specific organ that is damaged; for example, if hypertension is left untreated, it may cause renal insufficiency, which may then continue to deteriorate, causing kidney damage and leading to end-stage renal disease that requires dialysis.

Nonpharmacologic Treatment for Hypertension

Nonpharmacologic measures used to treat hypertension center around lifestyle changes. Lifestyle changes focus on the client's personal, social, and cultural influences. These changes may include diet modification, increased physical activity and exercise, smoking cessation, alcohol consumption reduction, relaxation techniques, and self-monitoring.

TRENDING TODAY

Gender and Racial Bias in Cardiovascular Disease Treatment

The AHA conducted a critical assessment of research and clinical knowledge on cardiovascular disease across the United States specifically addressing women's health. In its report to the president (https://openstax.org/r/heartorgennews), gaps were identified and actions outlined to optimize cardiovascular health in women across their lifespans, with the goal of reaching health equity in health care (Wenger et al., 2022). The AHA has deployed awareness campaigns that are culturally sensitive and focus on the optimization of preventive and clinical care. Community engagement and advocacy in policy change at the legislative level have been encouraged.

Access multimedia content (https://openstax.org/books/pharmacology/pages/18-1-hypertension-and-angina)
In a fireside video chat, *The Heart of the Matter: Racial and Gender Bias in Cardiovascular Care*, presented by Abbott Cardiovascular, an expert panel of health care providers and representatives discusses cardiovascular care. The panel identifies gender and racial bias as negatively impacting the client experience for persons with coronary and peripheral artery disease. The chat covers not only cardiovascular health but also technologies that may be utilized to bridge the critical gaps identified.

Dietary Modification

Clients with hypertension should eat a low-sodium diet consisting of whole grains, vegetables, and fruits. Other recommendations include low-fat dairy products and limiting meat intake to about two servings daily of lean meat, such as fish and poultry (Challa & Ameer, 2023). Reducing sweets and red meat is also important. The AHA (n.d.-b) recommends 1500 mg to no more than 2300 mg of sodium intake daily. Dietary patterns and nutritional therapy should focus on food preferences, social and cultural influences, and appropriate caloric intake.

Physical Activity and Exercise

The AHA (n.d.-d) recommends 150 minutes of moderate-intensity aerobic activity or 75 minutes of vigorous aerobic activity weekly. Average time for exercise should be at least 30–40 minutes per session to assist in decreasing blood pressure. If the client cannot do 30–40 minutes of moderate exercise four times a week, the nurse should suggest an alternate exercise plan, emphasizing that some physical activity is better than no physical activity. Physical activity and exercise enhance weight reduction and promote a healthy lifestyle.

Smoking Cessation and Reducing Alcohol Consumption

Tobacco use is the leading preventable cause of coronary artery disease. Smoking increases sympathetic nervous system activity, which causes vasoconstriction and, therefore, increases blood pressure, heart rate, and myocardial contractility. Although smoking has been established as a known risk factor for cardiovascular disease, its relationship to high blood pressure is still being investigated. Nevertheless, smoking and exposure to secondhand smoke contribute to increased accumulation of fatty deposits within the arteries, which high blood pressure is known to accelerate (AHA, n.d.-c).

Alcohol consumption increases blood pressure by increasing the level of the hormone renin in the blood. Renin decreases fluid elimination, causing higher fluid volume in the body and arterial vasoconstriction that results in an increase in blood pressure. Reducing alcohol consumption has been shown to decrease systolic and/or diastolic blood pressure by 5–12 mm Hg (Wake, 2021).

Relaxation Techniques

According to Harvard Health Publishing (2022), meditation has been associated with reducing blood pressure. Herawati et al. (2023) adds that slow breathing can be used as a nonpharmacological treatment to lower blood pressure. The National Center for Complementary and Integrative Health (2021) reviewed research on relaxation and blood pressure control that showed relaxation techniques resulted in small reductions in blood pressure and demonstrated yoga may be used as an adjunct intervention for the management of hypertension.

CLINICAL TIP

Assessing Client Lifestyle Modifications

The nurse should work closely with the client to promote lifestyle changes—such as diet modifications and weight loss, increase in exercise, smoking cessation, and use of relaxation techniques—that will improve baseline blood pressure readings.

Self-Monitoring of Hypertension

Home blood pressure monitoring (Figure 18.4) contributes to the comprehension of hypertension and facilitates the awareness of the importance of blood pressure management. Clients are now able to monitor their blood pressure with electronic blood pressure devices. Home blood pressure monitoring leads to awareness of one's blood pressure, better blood pressure control, and adherence to lifestyle changes and drug therapies (Verma et al., 2021).

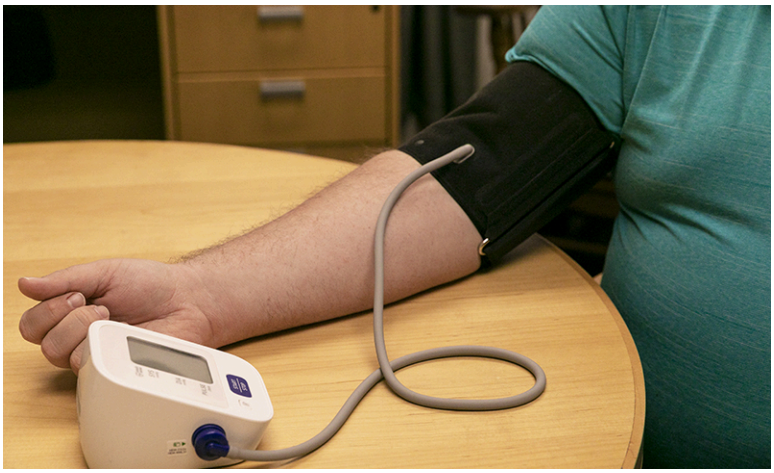


FIGURE 18.4 Daily blood pressure monitoring at home allows clients to better manage their blood pressure. (credit: "Arm Band Blood Pressure Monitor" by Alabama Extension/Flickr, Public Domain)

Pharmacologic Treatment of Hypertension

Pharmacologic treatment of hypertension centers on the individual client and takes into consideration their lifestyle as well as their personal, social, and cultural preferences. The objectives of pharmacological treatment are to reduce blood pressure and reduce the long-term effects of hypertension like organ damage. Angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, beta-adrenergic blockers, calcium channel blockers, and thiazide-like diuretics (Khalil & Zeltser, 2022) are the primary antihypertensive drugs used to treat high blood pressure. These drugs are discussed in detail later in this chapter.

CLINICAL TIP

Assessing Therapeutic Effects

The nurse should monitor the client's blood pressure to assess for drug efficacy. If blood pressure remains elevated despite antihypertensive treatment, the health care provider may adjust antihypertensive drugs to better control the client's blood pressure.

Angina

Angina (also called angina pectoris) is characterized by discomfort in the front of the chest, neck, shoulders, jaw, or arms that is precipitated by physical exertions and relieved by rest within 5 minutes or sublingual nitrates (Ueng et al., 2023). Angina is caused by reduced blood flow to the heart. The four types of angina (AHA, 2022a) are:

- Stable angina is the most common form. It often occurs during activity and may sometimes occur at rest. Stable angina is predictable and follows a pattern of similar episodes of chest pain.
- Unstable angina is unpredictable and considered a medical emergency. Unlike stable angina, unstable angina

usually occurs during rest and does not follow a pattern of similar episodes of chest pain; episodes may last longer than stable angina episodes. If blood flow to the heart does not improve, a myocardial infarction (heart attack) may occur.
- Variant (Prinzmetal) angina, unlike the other forms of angina, is not caused by coronary artery disease but rather by a spasm in the heart's arteries that temporarily decreases blood flow and almost always occurs at rest.
- Microvascular angina is frequent episodes of angina that occur due to coronary microvascular disease.

Risk factors for stable, unstable, and microvascular angina include age, family history, tobacco use, diabetes, hypertension, high cholesterol, obesity, and metabolic syndrome. Risk factors for Prinzmetal angina may be caused by anything that leads to spasms of the coronary arteries including certain medications such as decongestants, use of substances such as cannabis and cocaine, smoking tobacco, and stress (AHA, 2022a).

Pharmacologic Treatment of Angina

Pharmacologic treatment for angina is individualized. Client lifestyle, as well as social and cultural influences, impact the health care provider's treatment choice. The goal for pharmacologic treatment of stable angina is to prevent an ischemic event—like myocardial ischemia or infarction (heart attack)—from occurring. Nitrates are the first line of treatment for angina along with beta-adrenergic blockers and calcium channel blockers (Rousan & Thadani, 2019). Both types of blockers will be discussed further in this chapter.

UNFOLDING CASE STUDY

Part A

Read the following clinical scenario to answer the questions that follow. This case study will evolve throughout the chapter.

Hahn Tran is a 53-year-old client who presents to her health care provider's office with reports of a headache and dizziness. When questioned, she describes her headache as throbbing and that it is worse in the morning when she awakens. She is unable to identify any triggers for the headaches but states they are relieved with acetaminophen.

Hahn reports trying to follow a healthy diet but states that she does not really know what that means and that she uses a lot of salt in her cooking. She smokes about 6–8 cigarettes daily, which is down from one pack daily 3 months ago. Hahn does not exercise regularly and reports having 1–2 glasses of wine on the weekend. She lives with her husband and two teenage children and works in the kitchen at the children's school.

History
Hyperlipidemia
Type 2 diabetes

Current Medications
Atorvastatin, 20 mg once daily
Metformin, 500 mg twice daily

Vital Signs		Physical Examination
Temperature:	98.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Denies any changes in vision. No difficulty hearing conversations. • *Cardiovascular:* No jugular veindistention or pedal edema noted; S1, S2 heard on auscultation. Denies chest pain. Capillary refill brisk, mucous membranes pink and moist. • *Respiratory:* Lungs clear to auscultation. States she does not experience shortness of breath and sleeps on one pillow. Has been told she snores but denies apnea. • *GI:* Abdomen soft, nontender, nondistended; bowel sounds heard in all four quadrants. No report of nausea, vomiting, or abdominal pain. Has regular daily bowel movements. • *GU:* Deferred. • *Neurological:* Alert and oriented to time, place, person, and events. No reports of numbness, dizziness, vertigo, weakness, or seizures. • *Integumentary:* No wounds noted; skin appropriate for age.
Blood pressure:	168/96 mm Hg	
Heart rate:	88 beats/min	
Respiratory rate:	16 breaths/min	
Oxygen saturation:	97% on room air	
Height:	5'3"	
Weight:	184 lb	

TABLE 18.2

1. Based on the assessment, what diagnosis should the nurse anticipate from the health care provider?
    a. Elevated blood pressure
    b. Hypertension stage 1
    c. Hypertension stage 2
    d. Hypertensive crisis

2. Which of the following diagnostic tests would the nurse expect the health care provider to order for Hahn?
    a. Echocardiogram
    b. Cardiac catheterization
    c. Renal function panel
    d. Hepatic function panel

18.2 Angiotensin-Converting Enzyme (ACE) Inhibitors

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 18.2.1 Identify the characteristics of the angiotensin-converting enzyme inhibitor drugs used to treat hypertension.
- 18.2.2 Explain the indications, actions, adverse reactions, and interactions of the angiotensin-converting enzyme inhibitor drugs used to treat hypertension.
- 18.2.3 Describe nursing implications of angiotensin-converting enzyme inhibitor drugs used to treat hypertension.
- 18.2.4 Explain the client education related to angiotensin-converting enzyme inhibitor drugs used to treat hypertension.

Introduction and Use

Angiotensin-converting enzyme (ACE) inhibitors are a classification of drugs that block the body's production of angiotensin II. Angiotensin II induces oxidative stress and inflammation of cardiac tissue, which contributes to adverse remodeling processes. Angiotensin II also causes vasoconstriction and inhibits the reuptake of norepinephrine, stimulating catecholamine release. The release of catecholamine decreases urinary excretion of sodium and water, which then causes the release of aldosterone. Aldosterone stimulates the hypertrophy of the vascular smooth muscles, causing thickening of the vascular smooth muscle wall and restricting blood flow. ACE inhibitors (see Figure 18.5) are used to treat hypertension and cardiovascular diseases by reducing the release of aldosterone as part of the first line of treatment for clients who have hypertension (Goyal et al., 2022).

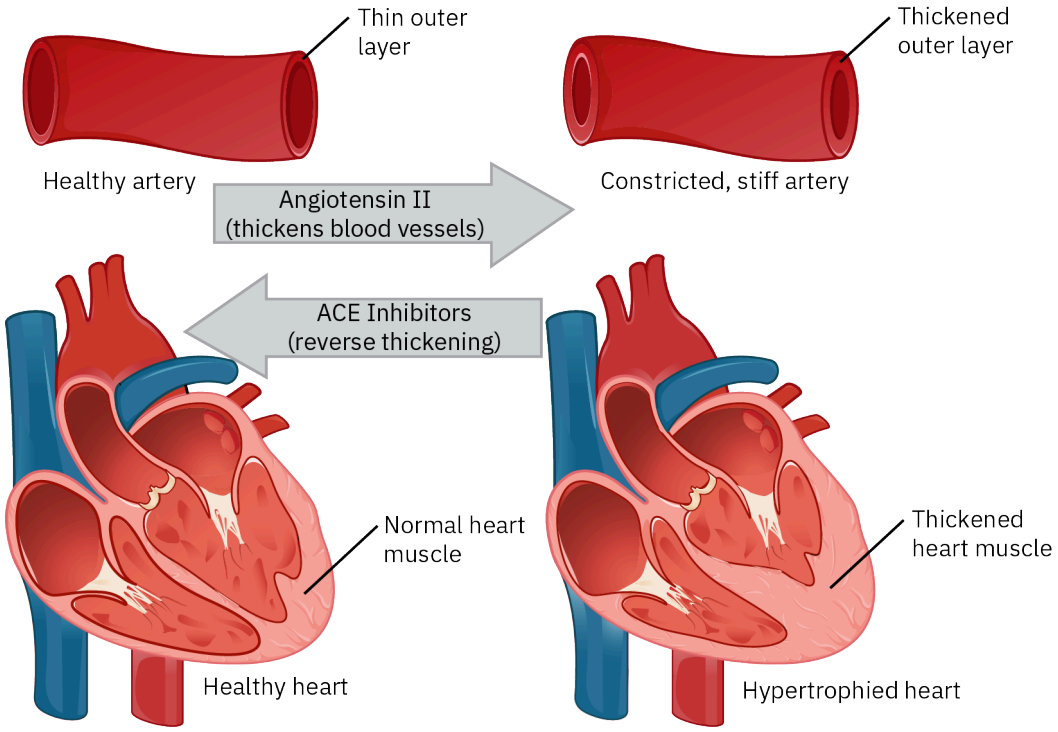


FIGURE 18.5 Angiotensin II constricts blood vessels; ACE inhibitors reverse thickening of the heart muscle. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license.)

SPECIAL CONSIDERATIONS

ACE Inhibitors

Some clients with hypertension demonstrate a lower response to ACE inhibitor monotherapy. ACE inhibitors interfere with the renin-angiotensin-aldosterone system, which causes high blood pressure when renin levels are high. Black clients often have hypertension, but also have lower levels of renin. Therefore, concomitant therapy may be required to increase response to antihypertensive therapies.

(Source: AstraZeneca, 2012)

Table 18.3 lists common ACE inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Benazepril (Lotensin)	10–40 mg orally daily.
Captopril (Capto)	25–150 mg orally 2–3 times daily; maximum dose 450 mg daily.
Enalapril (Vasotec)	5–40 mg administered in 1–2 daily doses. Initial dose: 5 mg orally once daily; maximum dose: 40 mg/day. May divide dose and administer twice daily.
Lisinopril (Zestril)	10–40 mg orally daily.

TABLE 18.3 Drug Emphasis Table: ACE Inhibitors (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

ACE inhibitors are relatively safe to use and have a low incidence of serious adverse effects. Adverse effects include angioedema, nonproductive cough, neutropenia (low neutrophils in the blood), agranulocytosis (low granulocytes in the blood), proteinuria (protein in the urine), and rash. Clients may develop an ACE inhibitor–associated cough (a persistent, dry, itchy cough), hyperkalemia (elevated potassium level in the blood), or hypotension (Jun et al., 2021).

ACE inhibitors should not be taken during pregnancy. Clients with renal impairment should use them cautiously. Clients with a previous hypersensitivity reaction to an ACE inhibitor should not be prescribed this classification of drug.

Table 18.4 is a drug prototype table for ACE inhibitors featuring enalapril. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Angiotensin-converting enzyme (ACE) inhibitor **Mechanism of Action** Inhibits the enzyme that converts angiotensin I to angiotensin II and thereby suppresses the renin-angiotensin-aldosterone system	**Drug Dosage** 5–40 mg administered in 1–2 daily doses. Initial dose: 5 mg orally once daily; maximum dose: 40 mg/day. May divide dose and administer twice daily.
Indications To control hypertension In the treatment of heart failure Treatment of acute myocardial infarction **Therapeutic Effects** Lowers blood pressure Increases blood supply and oxygen to the heart	**Drug Interactions** Aliskiren Sacubitril/valsartan Nonsteroidal anti-inflammatory drugs (NSAIDs) including selective cyclooxygenase-2 (COX-2) inhibitors Potassium-sparing diuretics Lithium Temsirolimus Sirolimus Everolimus **Food Interactions** No significant interactions
Adverse Effects Angioedema Fatigue Orthostatic hypotension Asthenia Diarrhea Nausea/vomiting Headache Dizziness/vertigo Hyperkalemia Cough Rash Abdominal pain Angina	**Contraindications** Hypersensitivity A history of angioedema related to previous treatment with an angiotensin-converting enzyme inhibitor or hereditary or idiopathic angioedema Pregnancy Caution: Aortic stenosis Diabetes Syncope Orthostatic hypotension Impaired renal function Breastfeeding

TABLE 18.4 **Drug Prototype Table: Enalapril** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ACE inhibitors:

- Assess the client's blood pressure and pulse on an ongoing basis with initial dosing and intermittently during drug therapy.
- Monitor serum potassium levels for hyperkalemia.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

SAFETY ALERT

ACE Inhibitors

Taking ACE inhibitors with potassium-containing salt substitutes or consuming large amounts of high potassium foods increases the risk of hyperkalemia. Having a blood potassium level above 6.0 mmol/L is considered a medical emergency and can result in cardiac arrest.

CLIENT TEACHING GUIDELINES

The client taking an ACE inhibitor should:

- Avoid foods high in potassium and salt substitutes (because these are high in potassium) due to the aldosterone release.
- Report side effects such as low blood pressure, cough, heart palpitations, nausea, vomiting, fever, chills, sore throat, swelling of the eyes and lips, or difficulty breathing to their health care provider.
- Notify their health care provider if pregnant, planning on getting pregnant, or breastfeeding before starting an ACE inhibitor.
- Report symptoms such as chest pain, slurred speech, hemiparesis, and difficulty speaking or walking to their health care provider immediately because these may be symptoms of a heart attack or stroke.
- Be aware that a persistent cough may develop when taking ACE inhibitors.

FDA BLACK BOX WARNING

ACE Inhibitors

The use of ACE inhibitors during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death.

18.3 Angiotensin II Receptor Blockers (ARBs)

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 18.3.1 Identify the characteristics of the angiotensin II receptor blocker drugs used to treat hypertension.
- 18.3.2 Explain the indications, actions, adverse reactions, and interactions of the angiotensin II receptor blocker drugs used to treat hypertension.
- 18.3.3 Describe nursing implications of angiotensin II receptor blocker drugs used to treat hypertension.
- 18.3.4 Explain the client education related to angiotensin II receptor blocker drugs used to treat hypertension.

Introduction and Use

Angiotensin II receptor blockers (ARBs) are a classification of drug that binds to and inhibits angiotensin II type I receptors. Renin secretion catalyzes the conversion of angiotensinogen to angiotensin in the liver where it is then converted to angiotensin II by the angiotensin-converting enzyme.

ARBs resemble ACE inhibitors in how they affect blood pressure and the cardiovascular system. However, there are three notable differences: ARBs are less likely than ACE inhibitors to cause a chronic cough (Carter, 2022); the risk of angioedema is decreased with ARBs as compared with ACE inhibitors; and ARBs have been shown to be effective in the treatment of chronic kidney disease and heart failure.

Table 18.5 lists common ARBs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Candesartan (Atacand)	16 mg orally daily; maximum dose 32 mg daily in 1–2 divided doses.
Losartan (Cozaar)	25–100 mg orally daily in 1–2 divided doses.
Telmisartan (Micardis)	40 mg orally daily initially; maximum dose 80 mg daily.
Valsartan (Diovan)	80–320 mg orally once daily.

TABLE 18.5 **Drug Emphasis Table: ARBs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of ARBs include dizziness, muscle cramps, weakness, heartburn, diarrhea, leg swelling, headaches, and weight loss. Serious adverse effects include angioedema, hypotension, hepatic impairment, and hyperkalemia.

SPECIAL CONSIDERATIONS

ARBs

The renin-angiotensin system has been associated with increased risk of mood disorders. The use of ARBs may be associated with an increased risk of suicide compared with other antihypertensive therapies (Sanches & Teixeira, 2021). Hypertensive clients with low renin (sometimes seen more often in Black clients) demonstrate a lower response to ARB monotherapy. Concomitant therapy may be required to increase response to antihypertensive therapies. Older adults (65 years and older) and clients with hepatic impairment should start on a low initial dose because ARBs are metabolized by the liver.

(Source: Colvin et al., 2020)

ARBs should not be taken during pregnancy. Clients with hepatic impairment should use ARBs cautiously. Clients with a previous hypersensitivity reaction or angioedema to an ARB should not be prescribed this classification of drug. Clients with a history of mood disturbances or who are at risk for mood disturbances should be monitored closely for suicidal ideation.

SAFETY ALERT

ARBs

ARBs can have teratogenic effects (causing harm to the embryo or fetus), so clients should avoid being pregnant while taking an ARB.

Table 18.6 is a drug prototype table for ARBs featuring valsartan. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Angiotensin II receptor blocker (ARB) **Mechanism of Action** Blocks the binding of angiotensin II to the angiotensin I receptor, thereby decreasing vasoconstriction and lowering blood pressure	**Drug Dosage** 80–320 mg orally daily.
Indications To control hypertension In the treatment of heart failure **Therapeutic Effects** Lowers blood pressure Increases blood supply and oxygen to the heart	**Drug Interactions** Aliskiren Spironolactone Triamterene Amiloride NSAIDs, including selective COX-2 inhibitors ACE inhibitors Lithium Potassium supplements Salt substitutes **Food Interactions** Alcohol Tobacco
Adverse Effects Hematuria Dizziness Syncope Increased thirst Decreased urinary output Irregular heartbeat Angioedema Hyperkalemia Orthostatic hypotension	**Contraindications** Hypersensitivity Concomitant use with aliskiren in clients with diabetes mellitus Pregnancy Caution: Hepatic impairment Renal impairment Hypotension Hypovolemia Hyperkalemia Breastfeeding

TABLE 18.6 **Drug Prototype Table: Valsartan** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ARBs:

- Monitor the client's blood pressure as prescribed.
- Monitor the client for interactions because many medications and herbal supplements interact with ARBs.
- Monitor the client for adverse effects, including electrolyte imbalances and alterations in liver and renal function.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ARB should:

- Avoid foods high in potassium and salt substitutes (because these are high in potassium).
- Report side effects such as low blood pressure, cough, heart palpitations, fever, chills, sore throat, swelling of lips or face, shortness of breath, or difficulty breathing to the health care provider.

- Notify their health care provider if they experience abdominal pain, joint or muscle aches, muscle weakness, change in the amount of urine produced, or trouble breathing.
- Notify their health care provider if pregnant, planning on getting pregnant, or breastfeeding before starting an ARB.

FDA BLACK BOX WARNING

ARBs

ARBs have the potential to harm or even kill a fetus if a client takes these drugs while pregnant.

18.4 Beta-Adrenergic Blockers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 18.4.1 Identify the characteristics of the beta-adrenergic blocker drugs used to treat hypertension.
- 18.4.2 Explain the indications, actions, adverse reactions, and interactions of the beta-adrenergic blocker drugs used to treat hypertension.
- 18.4.3 Describe nursing implications of beta-adrenergic blocker drugs used to treat hypertension.
- 18.4.4 Explain the client education related to beta-adrenergic blocker drugs used to treat hypertension.

Introduction and Use

Beta-adrenergic blockers (beta blockers) are a classification of drugs that inhibit chronotropic, inotropic, and vasoconstrictor response to catecholamine—such as epinephrine and norepinephrine—by exerting effects on adrenergic receptors beta 1, beta 2, and alpha.

Beta 1 receptors are found primarily in the heart and kidneys, and they increase the heart rate, myocardial activity, and release of renin. Beta 2 receptors are found in the smooth muscle tissue of the heart, lungs, and nervous system and increase myocardial contractility and cause muscle tremors. Alpha receptors stimulate vasoconstriction.

Beta blockers are classified as either nonselective or cardio-selective. Nonselective beta blockers affect both beta 1 and beta 2 and act on the cardiovascular and respiratory systems. Cardio-selective beta blockers, in contrast, affect beta 1, which impacts the cardiovascular system (Tucker et al., 2022).

Beta blockers decrease heart rate, decrease myocardial contractility, and decrease the rate of conduction through the atrioventricular (AV) node, thereby lowering blood pressure and heart rate. Beta blockers also cause vasodilation and decrease the release of renin and angiotensin II, promoting excretion of sodium and water from the body. Beta blockers are relatively safe for use. Beta blockers treat clients with hypertension, heart failure, arrhythmias, myocardial infarctions, migraines, glaucoma, and certain types of tremors. Beta blockers have also been used by health care providers as anxiolytics (to reduce anxiety).

Most beta blockers are taken orally. Labetalol, metoprolol, and propranolol can be administered intravenously. Extended-release beta blockers should not be crushed. Nurses should monitor blood pressure and pulse rate of clients using beta blockers. Beta blockers should not be administered if the client is hypotensive or has a heart rate of less than 60 (Farzam & Jan, 2022).

SPECIAL CONSIDERATIONS

Beta Blockers

Beta blockers pose an ethical dilemma for health care providers because they cause anxiolytic effects. The FDA, however, does not support this use for beta blockers. The health care provider may prescribe beta blockers *off-label* (against FDA-approved labeling indications for drug use) for anxiety. Therefore, the prescribed use of beta blockers for anxiolysis should be weighed against standards of practice as well as risks and benefits to the client.

(Source: Shahrokhi & Gupta, 2023)

Beta blockers may mask low blood sugar levels in clients with diabetes due to sympathetic nervous system inhibition.

(Source: Dungan et al., 2019)

Asthmatic clients and clients with chronic lung diseases should be monitored carefully while taking beta blockers because lung function can decrease due to beta 2 inhibition.

(Source: Huang et al., 2021)

Table 18.7 lists common beta blockers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Atenolol (Tenormin)	50 mg orally daily, either alone or with diuretic therapy. If optimal response is not achieved, the dosage should increase to 100 mg orally daily. Dosage beyond 100 mg a day is unlikely to produce any further benefit.
Carvedilol (Coreq)	6.25–25 mg orally twice daily; maximum dose 25 mg daily.
Metoprolol tartrate (Lopressor)	*Initial dosage:* 100 mg orally daily in single or divided doses. Increase dosage at weekly (or longer) intervals until optimum blood pressure reduction is achieved. *Effective dosage:* 100–450 mg daily.
Nadolol (Corgard)	40–320 mg orally daily.
Propranolol (Inderal LA)	40 mg orally twice daily; maximum dose 640 mg daily.

TABLE 18.7 **Drug Emphasis Table: Beta Blockers** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of beta blockers are dizziness, fatigue, weight gain, constipation, cold hands and feet, hypercholesterolemia, shortness of breath, depression, nausea, dry mouth, and dry eyes. Serious adverse effects include bradycardia, arrhythmias, hypoglycemia, and hypotension. Rare side effects include sexual and erectile dysfunction.

Beta blockers are contraindicated in clients with moderate to severe asthma and/or chronic lung diseases due to the potential for causing an exacerbation. Beta blockers should be used cautiously in clients with AV node and sinus bradycardia because they can aggravate these conditions. Beta blockers may exacerbate symptoms of Raynaud's phenomenon or cause this disease process in clients. People with diabetes should use beta blockers cautiously because they can mask the symptoms of hypoglycemia, causing confusion, fainting, or seizures.

Table 18.8 is a drug prototype table for beta-adrenergic blockers featuring metoprolol tartrate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Beta-adrenergic blocker **Mechanism of Action** Blocks beta 1 receptors, thereby decreasing cardiac workload by slowing the heart and decreasing the systolic blood pressure	**Drug Dosage** *Initial dosage:* 100 mg orally daily in single or divided doses. Increased dosage at weekly (or longer) intervals until optimum blood pressure reduction is achieved. *Effective dosage:* 100–450 mg daily.
Indications To control hypertension In the treatment of angina, acute myocardial infarction, and heart failure **Therapeutic Effects** Lowers blood pressure Decreases cardiac workload	**Drug Interactions** Albuterol Clonidine Mefloquine Calcium channel blockers Ma-huang Ephedra Black cohosh Hawthorne **Food Interactions** Caffeine Alcohol Tobacco Licorice
Adverse Effects Fatigue/weakness Dizziness Headache Hypotension Blurred vision Dry mouth Nausea/vomiting/diarrhea Drowsiness/insomnia Tinnitus Peripheral edema Erectile dysfunction	**Contraindications** Hypersensitivity AV block Cardiogenic shock Hypotension Acute heart failure Bradycardia Sick sinus syndrome Severe peripheral arterial circulatory disorders Caution: Thyroid impairment Hepatic impairment Asthma Peripheral vascular disease Diabetes mellitus Chronic obstructive pulmonary disease (COPD) Cerebrovascular disease

TABLE 18.8 **Drug Prototype Table: Metoprolol Tartrate** (source: https://dailymed.nlm.nih.gov/dailymed/)

CLINICAL TIP

Assessing Comorbidities: Asthma, Chronic Obstructive Pulmonary Disease, and Diabetes

Nurses should always assess a client's comorbidities—such as asthma, COPD, and diabetes—before administering beta blocker drugs. To prevent a pharmacological drug interaction, the nurse must assess whether clients are taking short-acting beta agonists (SABAs) because beta blockers can reduce their effectiveness. Additionally, nurses should be aware that beta blockers can mask the symptoms of hypoglycemia in clients with diabetes.

Nursing Implications

The nurse should do the following for clients who are taking beta-adrenergic blockers:

- Assess the client's blood pressure and pulse on an ongoing basis with initial dosing and intermittently during drug therapy.
- Do not administer the drug if the client's heart rate is less than 60 beats per minute and notify the health care provider.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a beta-adrenergic blocker should:

- Take their pulse as directed before taking a beta-adrenergic blocker and do not administer the drug if the pulse is less than 60 beats/minute or as directed by their health care provider.
- Understand that beta-adrenergic blockers can induce hyperglycemia. Clients with diabetes should monitor blood glucose levels closely.
- Take this medication without regard to meals.
- Report side effects such as bradycardia, hypotension, fatigue, dizziness, constipation, or sexual dysfunction to their health care provider.
- Monitor for symptoms of worsening heart failure such as fatigue, weight gain, and peripheral edema.

The client taking a beta-adrenergic blocker *should not:*

- Take beta-adrenergic blockers with over-the-counter (OTC) drugs or herbal supplements such as ma-huang, ephedra, black cohosh, hawthorn, or licorice without consulting their health care provider because these supplements may interfere with the action of the beta-adrenergic blocker.
- Discontinue use without speaking with the health care provider first because this may cause exacerbation of angina and myocardial infarction.

FDA BLACK BOX WARNING

Beta-Adrenergic Blockers

Beta blocker therapy should not be abruptly stopped but gradually tapered to avoid exacerbation of angina and myocardial infarction. Seek health care provider advice before discontinuing use.

18.5 Calcium Channel Blockers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 18.5.1 Identify the characteristics of the calcium channel blocker drugs used to treat hypertension and angina.
- 18.5.2 Explain the indications, actions, adverse reactions, and interactions of the calcium channel blocker drugs used to treat hypertension and angina.
- 18.5.3 Describe nursing implications of calcium channel blocker drugs used to treat hypertension and angina.
- 18.5.4 Explain the client education related to calcium channel blocker drugs used to treat hypertension and angina.

Introduction and Use

Calcium channel blockers are a classification of drug that blocks calcium from entering cells by binding to long-

acting voltage-gated calcium channels in the heart, smooth muscle, and pancreas. Calcium causes vasoconstriction. Calcium channel blockers inhibit calcium and allow for vasodilation, thereby causing the heart rate to slow and blood pressure to lower. Calcium channel blockers are commonly used to treat hypertension, angina, and arrhythmias.

Calcium channel blockers are classified as dihydropyridines or nondihydropyridines. Dihydropyridines are peripheral vasodilators that lower blood pressure and heart rate; they are used to treat post-intracranial hemorrhage, vasospasm, and migraines. In addition to their action on the peripheral vasculature, nondihydropyridines inhibit the sinoatrial and AV nodes, slowing cardiac conduction and heart rate and decreasing oxygen demand.

Calcium channel blockers may be used alone or in combination with other drugs. They are highly protein bound, which increases the volume of distribution within the body. Calcium channel blockers are available in long- and short-acting formulas.

SPECIAL CONSIDERATIONS

Calcium Channel Blockers

Calcium channel blockers are among the most effective antihypertensive classifications of drugs for use in non-Hispanic Black adults.

(Source: Abrahamowicz et al., 2023)

SAFETY ALERT

Calcium Channel Blockers

Abrupt discontinuation of calcium channel blockers may cause chest pain.

Table 18.9 lists common calcium channel blockers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Amlodipine (Norvasc)	5–10 mg orally daily.
Diltiazem (Cardizem)	*Initial dosage:* 30 mg orally 4 times daily, before meals and at bedtime. Increase dosage gradually (given in divided doses 3–4 times daily) at 1- to 2-day intervals until optimum response is obtained. *Average optimum dosage:* 180–360 mg daily.
Nicardipine (Cardene)	*Immediate release:* 20–40 mg orally 3 times daily. *Sustained release:* 30–60 mg daily; maximum dose 120 mg daily. *Intravenous (IV) infusion:* 5–15 mg hourly.
Nifedipine (Procardia)	*Immediate release:* Starting dose 10 mg orally 3 times daily. The usual effective dose range is 10–20 mg 3 times daily. Doses above 120 mg daily are rarely necessary. More than 180 mg daily is not recommended. *Sustained release:* 30–60 mg orally daily; maximum dose 120 mg daily.
Verapamil (Calan SR, Verelan)	*Immediate release:* 40–120 mg 3 times daily. *Sustained release:* 180–240 mg daily. *IV:* Follow manufacturer's instructions and health care provider's orders.

TABLE 18.9 **Drug Emphasis Table: Calcium Channel Blockers** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of calcium channel blockers include dizziness, constipation, palpitations, fatigue, flushing, nausea, rash, headache, and swelling in the legs and feet. Serious side effects include thrombocytopenia, hypotension, and hyperglycemia. Clients with a hypersensitivity to calcium channel blockers or their components should not use this

classification of drug. Other contraindications include sick sinus syndrome (except in clients with an artificial pacemaker), severe hypotension, a history of myocardial infarction, or a history of pulmonary congestion.

Table 18.10 is a drug prototype table for calcium channel blockers featuring amlodipine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Calcium channel blocker **Mechanism of Action** Inhibits the influx of calcium ions into vascular smooth muscle and cardiac muscle, thereby decreasing peripheral vascular resistance and reducing blood pressure	**Drug Dosage** 5–10 mg orally daily.
Indications To control hypertension In the treatment of angina **Therapeutic Effects** Lowers blood pressure Increases blood supply and oxygen to the heart	**Drug Interactions** Simvastatin Clarithromycin Ritonavir **Food Interactions** No significant interactions
Adverse Effects Peripheral edema Headache Fatigue Palpitations Hypotension Dizziness Nausea Flushing Pruritus Skin rash Muscle cramps Erectile dysfunction	**Contraindications** Hypersensitivity Caution: Aortic stenosis Symptomatic hypotension Angina Myocardial infarction Hepatic impairment Pregnancy Breastfeeding

TABLE 18.10 **Drug Prototype Table: Amlodipine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking calcium channel blockers:

- Monitor the client for interactions because many medications and herbal supplements, such as St. John's wort, interact with calcium channel blockers. Grapefruit juice also can affect the action of certain calcium channel blockers.
- Assess and monitor the client for adverse effects and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a calcium channel blocker should:

- Report side effects such as severe headaches, dizziness, lightheadedness, flushing, nausea, and leg swelling to their health care provider.
- Take this medication with food to avoid GI upset, nausea, and vomiting.

FDA BLACK BOX WARNING

Calcium Channel Blockers

Immediate release nifedipine, a potent calcium blocker, may increase the risk of myocardial infarction, stroke, and arrhythmias.

UNFOLDING CASE STUDY

Part B

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up to Case Study Part A.

Hahn Tran follows up with her health care provider one week later to get the results of her diagnostic studies. The health care provider diagnose her with hypertension stage 2 and starts her on enalapril, an ACE inhibitor. The nurse then teaches Hahn about this new drug.

3. Which instruction about enalapril will the nurse give Hahn?
   a. Take this medication with a meal.
   b. Do not take this medication if your heart rate is less than 60 beats/minute.
   c. Avoid salt substitutes that contain potassium while taking this medication.
   d. Avoid eating grapefruit while taking this medication.

4. Which nonpharmacologic treatment should the nurse anticipate the health care provider will prescribe for the client?
   a. Increase salt intake.
   b. Stop smoking.
   c. Walk 30–40 minutes twice weekly.
   d. Take naproxen sodium for headaches.

18.6 Diuretics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 18.6.1 Identify the characteristics of the diuretic drugs used to treat hypertension.
- 18.6.2 Explain the indications, actions, adverse reactions, and interactions of the diuretic drugs used to treat hypertension.
- 18.6.3 Describe nursing implications of diuretic drugs used to treat hypertension.
- 18.6.4 Explain the client education related to diuretic drugs used to treat hypertension.

Introduction and Use

Diuretics are a classification of drug that induces sodium loss and increases urine flow. They are typically used to treat hypertension, heart failure, and volume overload states. This chapter will cover diuretics as they are prescribed for hypertension and coronary heart disorders, thiazide and thiazide-like diuretics, and potassium-sparing diuretics. (Loop diuretics, which are also prescribed for heart failure, are discussed in Heart Failure Drugs.)

LINK TO LEARNING

FDA Blood Pressure Booklet (https://openstax.org/r/consumers)

The U.S. Food and Drug Administration (FDA) provides a client-oriented webpage listing FDA-approved products currently available to treat hypertension. It provides links to drug classifications such as ACE inhibitors, angiotensin II receptor blockers, beta blockers, calcium channel blockers, and diuretics. A high blood pressure

medicines booklet (https://openstax.org/r/govmeida) also is available for download.

Thiazide and Thiazide-Like Diuretics

Thiazide and thiazide-like diuretics inhibit the reabsorption of sodium and chloride in the distal renal tubules. These diuretics increase the excretion of sodium and water by the kidneys, producing diuresis in the client, and also create a potassium loss within the body. Along with ACE inhibitors, thiazide and thiazide-like diuretics are often the first line of treatment for clients diagnosed with hypertension and may be used in conjunction with other antihypertensive drugs (Akbari & Khorasani-Zadeh, 2022).

Potassium-Sparing Diuretics

Potassium-sparing diuretics antagonize aldosterone. These drugs reduce aldosterone-induced sodium and water retention in the late distal tubules of the kidneys. These types of diuretics retain potassium within the body; therefore, potassium does not need to be supplemented. Potassium-sparing diuretics are commonly used to treat hypertension and heart failure but should be used cautiously in clients with impaired renal function.

Table 18.11 lists common diuretics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Chlorthalidone (Thalitone)	25–100 mg orally daily; maximum dose 100 mg daily.
Hydrochlorothiazide (Microzide)	12.5–50 mg orally daily.
Amiloride (Midamor)	5–20 mg orally daily; maximum dose 20 mg daily.
Spironolactone (Aldactone)	25–100 mg orally daily
Triamterene (Dyrenium)	Individualized based on client need. When used alone, the starting dose is 100 mg orally twice daily. Maximum dose should not exceed 300 mg orally daily.

TABLE 18.11 **Drug Emphasis Table: Thiazide-Like and Potassium-Sparing Diuretics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Diuretics are used to treat various disorders. Common adverse effects include mineral loss, weakness, fatigue, muscle cramps, palpitations, dizziness, and electrolyte imbalances. Adverse effects from hypokalemia (with thiazide and thiazide-like diuretics) and hyperkalemia (with potassium-sparing diuretics) are potentially severe and/or fatal. Clients with a hypersensitivity to diuretics or their components should not take this classification of drugs. Diuretics should be used cautiously in older clients and clients with hepatic or renal impairment, arrhythmias, or gout.

Table 18.12 is a drug prototype table for diuretics featuring hydrochlorothiazide (a thiazide diuretic). It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Thiazide diuretic **Mechanism of Action** Inhibits sodium chloride transport in the distal convoluted tubules, thereby causing increased sodium excretion in the kidneys and lowering blood pressure	**Drug Dosage** 12.5–50 mg orally daily.
Indications To control hypertension To control edema **Therapeutic Effects** Lowers blood pressure Decreases edema	**Drug Interactions** Dofetilide Antidiabetic drugs Barbiturates Cholestyramine NSAIDs Lithium **Food Interactions** Alcohol Tobacco
Adverse Effects Blurred vision Chills/cold sweats Headache Joint pain/stiffness Nausea/vomiting Sore throat Trembling Weakness Stevens Johnson syndrome	**Contraindications** Anuria, hypersensitivity Caution: Orthostatic hypotension Impaired renal function Pregnancy Breastfeeding

TABLE 18.12 **Drug Prototype Table: Hydrochlorothiazide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking diuretics:

- Assess the client's blood pressure and pulse on an ongoing basis with initial dosing and intermittently during drug therapy.
- Assess the client for electrolyte imbalances and hyperglycemia as well as the client's urine output. Urine output for an adult should be weight based at 0.5 mL/kg/hour.
- Assess and monitor for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See the chart below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a diuretic should:

- Take diuretics early in the morning to avoid increased urination during the night and sleep disturbance.
- Take diuretics with food to avoid GI upset, nausea, and vomiting.
- Report a weight loss or weight gain greater than 2 pounds a day or 5 pounds a week to their health care provider.

The client taking a thiazide/thiazide-like diuretic should:

- Report side effects such as low blood pressure, fatigue, bleeding, hypokalemia, weakness, rash, and leg cramps to their health care provider.

- Eat potassium-rich foods such as avocados, bananas, and spinach to replace potassium.
- If diabetic, monitor their blood glucose levels carefully due to these diuretics' effects on carbohydrate metabolism.

The client taking a potassium-sparing diuretic should:

- Avoid exposure to direct sunlight because spironolactone can cause photosensitivity.
- Avoid potassium-rich foods such as avocados, bananas, beans, and spinach if their potassium levels are high.

18.7 Nitrates

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 18.7.1 Identify the characteristics of the nitrate drugs used to treat hypertension and angina.
- 18.7.2 Explain the indications, actions, adverse reactions, and interactions of the nitrate drugs used to treat hypertension and angina.
- 18.7.3 Describe nursing implications of nitrate drugs used to treat hypertension and angina.
- 18.7.4 Explain the client education related to nitrate drugs used to treat hypertension and angina.

Introduction and Use

Nitrates are a classification of drugs that cause vasodilation of blood vessels, which relaxes smooth muscles and causes the dilation of coronary vessels. Vasodilation improves oxygen supply to the heart, decreases oxygen demand within the body, reduces cardiac workload (preload and afterload), and lowers blood pressure. Nitrates have been used to treat chest pain and angina since the early 1800s. Nitrates come in different forms including oral, sublingual, translingual spray, intravenous, topical, and transdermal and can be short-acting or long-acting. Nitrates are commonly used to treat angina, acute coronary syndrome, arterial hypertension, and heart failure (Lee & Gerriets, 2022).

SPECIAL CONSIDERATIONS

Nitrates

Older clients using nitrates are at a higher risk for postural hypotension and should rise from a lying or sitting position slowly to prevent falls and injuries.

(Source: Lee & Gerriets, 2023)

Table 18.13 lists common nitrates and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Isosorbide dinitrate (Isordil)	*Sublingual tablets:* 2.5–10 mg by sublingual route as needed every 2–4 hours. *Immediate-release tablets:* 5–80 mg orally 2–3 times daily. *Sustained-release capsules:* 40 mg orally 1–2 times daily; maximum dose 160 mg daily.
Isosorbide mononitrate (Imdur)	*Immediate-release tablets:* 5–20 mg twice daily. *Extended-release tablets:* 30–60 mg once daily; maximum dose 240 mg daily.

TABLE 18.13 Drug Emphasis Table: Nitrates (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Nitroglycerin (Nitrobid, Nitrostat, Nitrolingual)	*Sublingual tablets:* 0.15–0.6 mg administered sublingually as needed for chest pain every 5 minutes up to 3 times for continued chest pain. *Sustained-release tablets:* 2.5 mg orally 3–4 times daily. *Spray:* 1–2 metered doses (0.4 mg/dose) sprayed onto oral mucosa as needed for chest pain every 5 minutes up to 3 times for continued chest pain. *Ointment:* 1/2 to 2 inches applied topically every 4–8 hours daily. *Patch (disk):* Applied to skin once daily. *Solution:* 5–10 mcg/minute up to 100 mcg/minute IV.
Nitroprusside (Nipride)	*Solution:* 0.3 mcg/kg/min IV and titrate every few minutes until desired effect is achieved; maximum dose 10 mcg/kg/min.

TABLE 18.13 Drug Emphasis Table: Nitrates (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects for nitrates include headache, lightheadedness, flushing, syncope, reflex tachycardia, and dizziness. Serious adverse effects include hypotension.

Contraindications include allergies to nitrates, concomitant use of phosphodiesterase (PDE) inhibitors such as tadalafil and sildenafil, history of right ventricular infarction, and hypertrophic cardiomyopathy. Nitrates should be used cautiously in clients on long-term diuretic therapy, with low systolic blood pressure, with autonomic nervous system dysregulation, and who are pregnant or breastfeeding.

SAFETY ALERT

Nitrates

Nitrates can induce hypotension. They should not be taken with PDE inhibitors because they can cause severe hypotension and cardiac decompensation.

Table 18.14 is a drug prototype table for nitrates featuring nitroglycerin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nitrate **Mechanism of Action** Relaxes the smooth muscles and blood vessels, causing vasodilation, and thereby lowering blood pressure, heart rate, and cardiac workload	**Drug Dosage** *Sublingual tablets:* 0.15–0.6 mg administered sublingually as needed for chest pain every 5 minutes up to 3 times for continued chest pain. *Sustained-release tablets:* 2.5 mg orally 3–4 times daily. *Spray:* 1–2 metered doses (0.4 mg/dose) sprayed onto oral mucosa as needed for chest pain every 5 minutes up to 3 times for continued chest pain. *Ointment:* 1/2 to 2 inches applied topically every 4—8 hours daily. *Patch (disk):* Applied to skin once daily. *Solution:* 5–10 mcg/minute up to 100 mcg/minute IV.
Indications To control angina In the treatment of hypertensive emergency, pulmonary edema, and heart failure **Therapeutic Effects** Lowers blood pressure Decreases cardiac workload	**Drug Interactions** Avanafil Riociguat Sildenafil Tadalafil Vardenafil **Food Interactions** Alcohol Tobacco
Adverse Effects Orthostatic hypotension Tachycardia Paradoxical bradycardia Flushing Peripheral edema Nausea/vomiting Headache Blurred vision Syncope Palpitations	**Contraindications** Hypersensitivity Increased intracranial pressure Cardiomyopathy Shock Caution: Hepatic impairment Renal impairment Myocardial infarction Hypotension Hypovolemia Head trauma Pregnancy Breastfeeding

TABLE 18.14 **Drug Prototype Table: Nitroglycerin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking nitrates:

- Carefully assess the client for drug and herbal supplement interactions because they may cause profound hypotension.
- Assess and monitor the client's blood pressure during initial dosing and intermittently throughout drug therapy, especially if administering nitrates intravenously, because they may cause severe hypotension.
- Do not administer nitrates if the client's systolic blood pressure is less than 90 mm Hg and if the heart rate is greater than 100 beats/minute. Notify the health care provider.
- Adhere to health care provider instructions on how and when to administer this classification of drug or when to hold the drug.
- Assess adverse effects and therapeutic effects.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client

teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a sublingual nitrate should:

- Take sublingual nitrates if chest pain occurs. They should take one sublingual nitrate every 5 minutes times three doses if chest pain persists. If chest pain continues, the client should call 911.
- Store sublingual nitrate bottles away from the light in a dry place and in the original amber glass bottle.

The client using nitrate patches should:

- Apply patches once daily as a maintenance medication.
- Avoid hairy areas when applying nitrate patches.
- Remove nitrate patches for 10–12 hours before placing a new one to prevent tolerance.
- Rotate sites of nitrate patches to prevent skin irritation.

The client using a nitrate *should not:*

- Use patches for acute chest pain.
- Take erectile dysfunction medications because this may cause profound hypotension.

Other Concerns

- Headaches may occur with the use of nitrates. Acetaminophen may help in relieving these headaches.
- If low blood pressure develops, the client should lie on their back with legs elevated and notify their health care provider.

FDA BLACK BOX WARNING

Nitroprusside

Nitroprusside can cause precipitous decreases in blood pressure which can lead to irreversible ischemic injuries or death.

Nitroprusside produces dose-related cyanide which can be lethal. Limit infusions at the maximum rate to as short as duration as possible.

UNFOLDING CASE STUDY

Part C

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up from Case Study Parts A and B.

Hahn Tran is following up with the health care provider 3 months after her initial diagnosis of hypertension stage 2. She reports her headaches and dizziness have improved; however, she is now reporting chest pain when she walks 1–2 miles. The chest pain is relieved by resting on a park bench. Hahn states she experiences a burning in her chest that does not radiate to other areas. She denies nausea, diaphoresis, shortness of breath, or dizziness with chest pain.

The nurse performs a 12-lead ECG on Hahn, as ordered. The health care provider notes that there are no ischemic changes and diagnoses Hahn with stable angina. The health care provider prescribes verapamil 40 mg orally three times daily and nitroglycerin 0.4 mg sublingually for chest pain. The nurse is developing a teaching care plan for Hahn.

Vital Signs		Physical Examination
Temperature:	98.4°F	• *Cardiovascular:* No jugular vein distention or pedal edema; S1, S2 noted. • *Respiratory:* Breath sounds clear on auscultation.
Blood pressure:	144/90 mm Hg	
Heart rate:	78 beats/min	
Respiratory rate:	16 breaths/min	
Oxygen saturation:	98% on room air	
Height:	5'3"	
Weight:	188 lb	

TABLE 18.15

5. Which instruction about verapamil will the nurse include in the teaching plan?
   a. Limit your fluid intake when taking this medication.
   b. Do not take this medication on an empty stomach.
   c. Swelling of your feet is common when taking this medication.
   d. Increase your daily fiber intake when taking this medication.

6. The nurse teaches Hahn about a heart-healthy diet. Which statement by Hahn indicates a need for further teaching?
   a. “I can eat red meat every day.”
   b. “I need to reduce my salt intake.”
   c. “Apples and oranges are a good snack option.”
   d. “I can replace table salt with dried herbs.”

Chapter Summary

This chapter focused on antihypertension and antianginal drugs. Hypertension and angina were defined. Stroke volume and peripheral vascular resistance are the two determinants of blood pressure. The renin-angiotensin-aldosterone system was described, and how it impacts blood pressure within the body was explained. Blood pressure guidelines by the American Heart Association were discussed. The types of angina were briefly explained along with typical findings.

Common antihypertensive and antianginal drug classifications were covered in the chapters. Drug classifications covered included ACE inhibitors, ARBs, beta-adrenergic blockers, calcium channel blockers, diuretics, and nitrates. These drug classifications are used as mono- or multi-drug treatment therapy for hypertension and angina.

Key Terms

aldosterone a hormone made in the adrenal cortex that helps to control the balance of water and salts in the kidneys, retaining sodium and releasing potassium from the body

angina chest discomfort in the front of the chest, neck, shoulders, jaw, or arms that is precipitated by physical exertions and relieved by rest or sublingual nitrates

angiotensin I a protein in blood that promotes aldosterone secretion and raises blood pressure

angiotensin II a protein in the blood that causes the muscular walls of the arterioles to constrict and narrow, thereby increasing blood pressure

angiotensin II receptor blocker (ARB) a classification of drug that binds to and inhibits angiotensin II type I receptors

angiotensin-converting enzyme (ACE) inhibitor a classification of drug that blocks the body's production of angiotensin II; the protein that causes vasoconstriction and inhibits the reuptake of norepinephrine, which stimulates catecholamine release

antianginal drugs drugs used in the treatment of angina

antihypertensive drugs drugs used in the treatment of hypertension

beta-adrenergic blocker a classification of drug that inhibits chronotropic, inotropic, and vasoconstrictor response to catecholamine, epinephrine, and norepinephrine by exerting effects on adrenergic receptors beta 1, beta 2, and alpha.

calcium channel blocker a classification of drug that blocks calcium from entering cells by binding to long-acting voltage-gated calcium channels in the heart, smooth muscle, and pancreas

cardiac output the product of the heart rate and stroke volume; the volume of blood pumped by the heart per unit of time, usually measured in liters per minute

diastolic blood pressure indicates how much pressure the blood is exerting against artery walls while the heart is resting between beats; the second number of a blood pressure reading

diuretic a classification of drug that induces sodium loss and increases urine flow; typically used to treat hypertension, heart failure, and volume overload states

heart rate the number of times each minute the heart beats

hypertension when an individual's blood pressure is above the normal limits for a sustained period of time

hypotension when an individual's blood pressure is below the normal limits for a sustained period of time

nitrate a classification of drug that causes vasodilation of blood vessels by imparting nitric oxide, which relaxes smooth muscles

peripheral vascular resistance determined by blood flow in the body and the level of constriction or dilatation within the vessels

renin-angiotensin-aldosterone system (RAAS) a compensatory mechanism the body activates during hypotension (when the blood pressure is low)

stroke volume the volume of blood pumped out of the left ventricle of the heart during each systolic cardiac contraction

systolic blood pressure indicates how much pressure the blood is exerting against the artery walls when the heart beats; the first number of a blood pressure reading

vasopressin an antidiuretic hormone that regulates blood pressure, blood osmolality, and blood volume

Review Questions

1. A client has a blood pressure of 148/96 mm Hg. According to the American Heart Association Guidelines, how should the nurse classify this blood pressure?

a. Normal
b. Elevated
c. Hypertension stage 1
d. Hypertension stage 2

2. A home health nurse is monitoring a client who has a history of hypertension and is taking benazepril. Which outcome indicates a therapeutic effect of the medication?
a. Heart rate of 96 beats/minute
b. Blood pressure of 126/76 mm Hg
c. Potassium level of 5.1 mEq/dl
d. Dry cough and fatigue

3. A nurse is reviewing the health history of a client with hypertension and coronary artery disease. The health care provider is considering a beta-adrenergic blocker, nadolol, for the client. Which condition in the client's health history should the nurse report to the health care provider as a contraindication for nadolol?
a. Asthma
b. Hypertension
c. Tachycardia
d. Myocardial infarction

4. The health care provider's order is for metoprolol 0.1 g orally daily. The tablets are available in 50 mg. How many tablets should the nurse administer?
a. 1 tablet
b. 2 tablets
c. 4 tablets
d. 5 tablets

5. A client with newly diagnosed stable angina is prescribed transdermal nitroglycerin. Which instruction should the nurse include in client teaching?
a. Apply to the same area of the body every day.
b. Apply a new patch at the onset of chest pain.
c. Apply a new patch after showering while skin is still moist.
d. Apply the patch for 12–14 hours and then remove for 10–12 hours.

6. A nurse is providing education to a client who has a new prescription for verapamil. The nurse should instruct the client to avoid which beverage when taking verapamil?
a. Milk
b. Coffee
c. Tomato juice
d. Grapefruit juice

7. A nurse is teaching a client with newly diagnosed hypertension about a prescription for hydrochlorothiazide. Which instruction should the nurse include in the client teaching?
a. Take this medication at bedtime.
b. Monitor for leg cramps.
c. Avoid citrus juices.
d. Reduce your intake of potassium-rich foods.

8. The nurse is to administer carvedilol 6.25 mg orally twice daily. The tablets available contain 3.125 mg. How many tablets will the client receive per dose?
a. 1 tablet
b. 2 tablets
c. 3 tablets

d. 4 tablets

9. A client is being prescribed losartan at discharge from the hospital by the health care provider. The discharge instructions by the nurse should include what information about how losartan acts?
   a. It inhibits beta 1 and beta 2.
   b. It inhibits angiotensin-converting enzyme.
   c. It prevents the release of angiotensin.
   d. It blocks angiotensin II from angiotensin I receptors.

10. A nurse is preparing to administer carvedilol to a client with hypertension. Which assessment finding should the nurse report to the health care provider before administering the drug?
   a. Apical heart rate 56 beats/minute
   b. Blood pressure 114/74 mm Hg
   c. Temperature 98.6°F
   d. Respiratory rate 18 breaths/minute

CHAPTER 19
Heart Failure Drugs

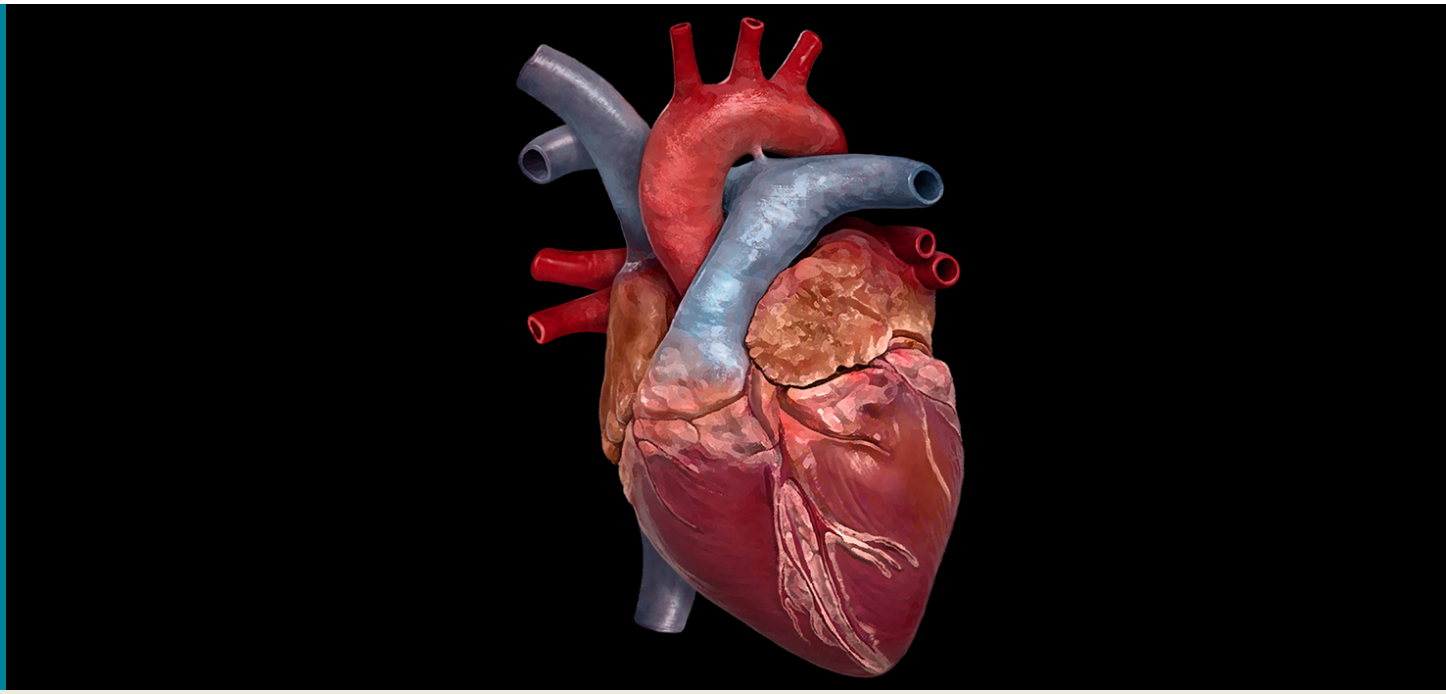


FIGURE 19.1 The heart is the primary organ of the cardiovascular system, controlling circulation and blood flow for the entire body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Heart failure is a complex syndrome that occurs when the heart is no longer able to generate adequate cardiac output. Anything that affects left ventricular filling or pumping can lead to heart failure, and it is often the result of prolonged untreated hypertension or acute myocardial infarction. This chapter will review heart failure and the pharmacologic and nonpharmacologic treatments for this syndrome.

19.1 Heart Failure

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 19.1.1 Describe the pathophysiology of heart failure and ventricular dysfunction.
- 19.1.2 Identify clinical manifestations associated with heart failure and ventricular dysfunction.
- 19.1.3 Identify etiology and diagnostic studies related to heart failure and ventricular dysfunction.

Pathophysiology of Heart Failure

The importance of cardiac output cannot be stressed enough; it is necessary for every organ in the body. **Cardiac output** is a function of heart rate (HR) and stroke volume (SV): $\mathrm{CO} = \mathrm{HR} \times \mathrm{SV}$. Normal resting CO is 4–5 liters per minute. **Heart rate** is the number of times the heart beats per minute. **Stroke volume** is the amount of blood

pumped out of the left ventricle with each heartbeat. Stroke volume is a function of preload, afterload, and contractility. **Preload** is the volume of blood returning to the heart, **afterload** is the amount of pressure that the left ventricle must push against, and **contractility** is the ability of the left ventricle to squeeze or pump blood. Stroke volume is often measured by **ejection fraction**, or the percentage of blood that is pumped out of the left ventricle with each beat (Hajouli & Ludhwani, 2022). It is important to note that the entire volume of the left ventricle is not pumped out with each beat; a small portion remains in the chamber. Factors affecting cardiac output can be seen in Figure 19.2.

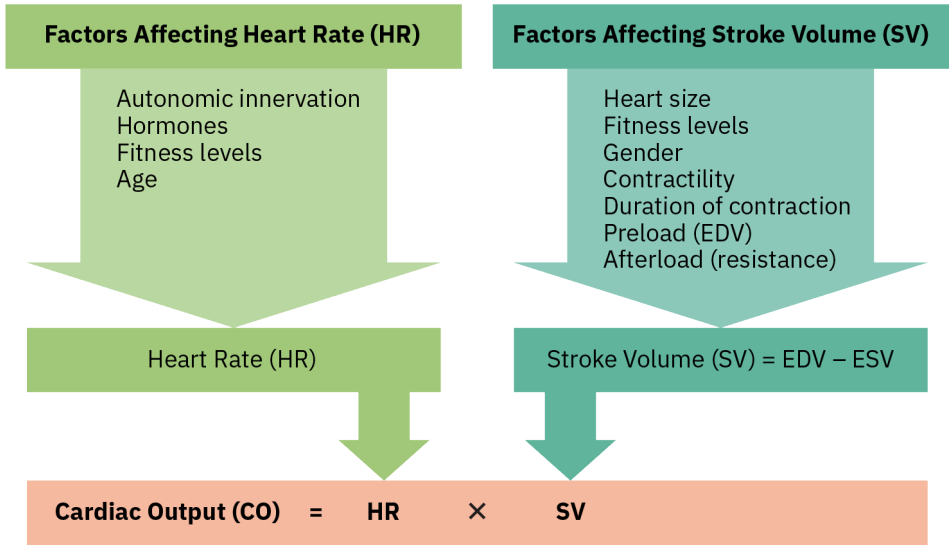


FIGURE 19.2 Cardiac output is influenced by heart rate and stroke volume, both of which are variable. (Note: EDV: End diastolic volume; ESV: End systolic volume.) (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

In order for the heart to produce adequate stroke volume, the left ventricle must be able to fill well (preload) and squeeze well (contractility). Contractility requires adequate muscle tissue (adequate cardiac myocytes), which must receive an adequate blood supply. So, the heart itself is dependent on cardiac output.

Heart failure occurs when the heart is no longer able to generate an adequate cardiac output. Heart failure is a result of ventricular dysfunction; something has affected ventricular preload or contractility in such a way that the ventricle is no longer able to expel blood effectively (Malik et al., 2022). This leads to decreased perfusion of all tissues. There are two ways in which the heart is not able to maintain cardiac output. One is caused by a reduced ejection fraction and is called **heart failure with reduced ejection fraction (HFrEF)**. The other, called **heart failure with preserved ejection fraction (HFpEF)**, occurs when the actual ejection fraction is not reduced but cardiac output is still decreased.

Heart Failure with Reduced Ejection Fraction

Heart failure with reduced ejection fraction is a problem stemming from inadequate contractility. It is the most common type of heart failure. There are multiple causes of HFrEF, including coronary artery disease and acute myocardial infarction (AMI). Both cause decreased oxygenation to the individual cardiac muscle cells or cardiac myocytes. Because the cardiac myocytes have less oxygen than they need, they are not able to contract well. In the case of an AMI, the myocytes have had their oxygen supply cut off, and so there is cell death. Dead myocytes don't contract at all.

Hypertension is also a common cause of HFrEF. Long-standing untreated hypertension increases afterload and causes the left ventricle to work harder to eject blood. Initially, the left ventricle can hypertrophy (thicken) to push against the increased resistance (see Figure 19.3). After many years, the left ventricular hypertrophy can't keep up with the increased resistance, and the heart is unable to maintain an adequate cardiac output. Because contractility and afterload are considered part of systole, this was traditionally referred to as *systolic heart failure*.

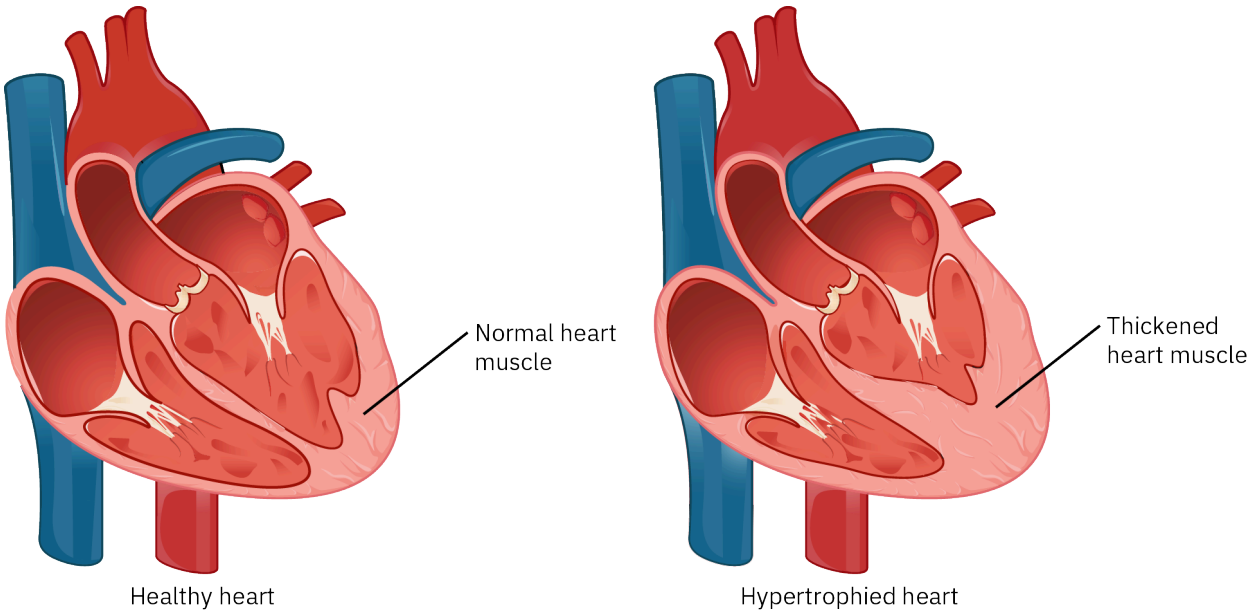


FIGURE 19.3 The heart muscle thickens during heart failure. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Heart Failure with Preserved Ejection Fraction

Heart failure with preserved ejection fraction stems from muscle stiffness. As people age, muscles can become stiff and not move as well as they did in younger years. This also can happen to the left ventricle; the muscle tissue can become stiff, which does not allow for adequate ventricular opening. If the ventricles cannot open well, then they cannot fill well. If the ventricle cannot fill well, this decreases preload, which then decreases stroke volume.

Recall that ejection fraction (EF) is the percentage of blood pumped from the heart with each beat (EF is defined as blood ejected from the left ventricle divided by total volume of blood in the left ventricle at the end of diastole). In HFpEF, less blood fills the ventricle during diastole (thus there is lower total volume at the end of diastole/lower preload, the denominator in the above equation), and less blood is pumped out of the left ventricle (lower stroke volume and thus lower cardiac output, the numerator in the above equation). Therefore, both the denominator and numerator of the equation change proportionally and the ratio, or ejection fraction, remains the same despite cardiac output being lower. Hence the name heart failure with preserved ejection fraction. Because preload is considered part of diastole (or ventricular filling), this type of heart failure traditionally was referred to as *diastolic heart failure*.

The main treatment for HFpEF is control of hypertension and other comorbidities, if present. (Hypertension is discussed in more detail in Antihypertensive and Antianginal Drugs.) Nearly all pharmacologic treatments for heart failure are specific to heart failure with reduced ejection fraction. The Pharmacologic Treatment of Heart Failure section will pertain to heart failure with reduced ejection fraction.

Classification and Staging of Heart Failure

Heart failure is diagnosed based on ejection fraction and symptoms. The American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America (HFSA) Guidelines state that a normal ejection fraction is between 50% and 70% (Heidenreich et al., 2022). If a person has an ejection fraction of less than 40%, a diagnosis of heart failure with reduced ejection fraction is made. Heart failure with mildly reduced ejection fraction means that a person has symptoms of heart failure but the ejection fraction is between 41% and 50%. Heart failure with preserved ejection fraction is diagnosed when there are symptoms of heart failure but the ejection fraction is still in the normal range (see Table 19.1).

Type of Heart Failure	Criteria
Heart failure with reduced ejection fraction (HFrEF)	Left ventricular ejection fraction ≤40%
Heart failure with mid-range ejection fraction (HFmrEF)	Left ventricular ejection fraction 41%–49% with symptoms of heart failure
Heart failure with preserved ejection fraction (HFpEF)	Left ventricular ejection fraction ≥50% with symptoms of heart failure

TABLE 19.1 Classification of Heart Failure by Left Ventricular Ejection Fraction (LVEF) (source: Heidenreich et al., 2022)

Heart failure is staged based on risk and evidence of structural damage (see Table 19.2). The Pharmacologic Treatment of Heart Failure section will pertain to Stage C: Symptomatic Heart Failure.

Stage A At Risk for Heart Failure	Stage B Pre–heart Failure	Stage C Symptomatic Heart Failure	Stage D Advanced Heart Failure
Clients are at risk for heart failure but don't have signs or symptoms or any damage to the pumping ability of the heart.	Clients don't have signs or symptoms of heart failure but do have some type of damage to the pumping ability of the heart.	Clients have signs and/or symptoms of heart failure and have damage to the pumping ability of the heart.	Clients have significant signs and/or symptoms of heart failure that interrupt activities of daily living and often cause hospitalization.

TABLE 19.2 ACC/AHA/HFSA Stages of Heart Failure (source: Heidenreich et al., 2022)

Diagnostics

It can be difficult to diagnose heart failure because it is based on symptom recognition. People often have symptoms but don't recognize them as a manifestation of heart failure. In order for heart failure to be diagnosed, a health care provider must do a thorough history and physical exam. If there are signs and symptoms of heart failure, the provider will order an echocardiogram. In an echocardiogram, sound waves are used to assess how well the heart is pumping and to determine the heart's ejection fraction. Other tests that may be performed include an electrocardiogram to assess cardiac rhythm and blood work. Typical blood work includes a basic metabolic profile, which will include information on electrolytes and kidney function. One other blood test that is often included is a brain natriuretic peptide (BNP) to determine whether the heart is undergoing increased stretch. When cardiac myocytes are stretched too far, they release BNP (Novack & Zevitz, 2022). This test often helps providers determine the stage of heart failure.

Clinical Manifestations

Heart failure often occurs after another disease process has damaged the cardiovascular system. The most common causes of HFrEF are coronary artery disease, acute myocardial infarction, and prolonged hypertension. The most common cause of HFpEF is aging. Therefore, heart failure is often a disease of older clients, though it is not exclusive to that age group. Symptoms associated with heart failure include shortness of breath, edema, exercise intolerance, and fatigue. Often people with heart failure have an increased heart rate due to the body's compensatory mechanisms. Remember: $\mathrm{CO} = \mathrm{HR} \times \mathrm{SV}$. If stroke volume is decreased, then the body will compensate by increasing heart rate.

Nonpharmacologic Treatment of Heart Failure

Nonpharmacologic treatments for heart failure include sodium restriction. A sodium-restricted diet (less than 2000 mg of sodium per day) may help maintain euvolemia (normal blood volume) and prevent clients from becoming overloaded with fluid (which presents as pitting edema in the extremities, abdominal edema, and/or pulmonary edema). It is also important for people with heart failure to eat a healthy diet and exercise as well as they are able. Additionally, smoking cessation, reduced or no use of alcohol, and self-monitoring of signs and symptoms may be helpful.

Dietary Modification

Dietary modification for clients with heart failure are similar to those for clients with hypertension (see

Antihypertensive and Antianginal Drugs). Clients with heart failure should follow a 2000 mg/day sodium-restricted diet and are often instructed to record the amount of sodium they consume daily. Clients should be instructed on how to read Nutrition Facts labels on food in order to determine the amount of sodium per serving or per container. Clients should be made aware that most processed foods are very high in sodium. Fast food, processed frozen meals, and canned foods all have very high sodium content. The client can be referred to the American Heart Association's recipe collection (https://openstax.org/r/recipesheart) for low-sodium, heart-healthy meals.

Clients who take certain medications for heart failure (discussed later in this chapter) should be instructed to avoid foods high in potassium, such as bananas and watermelon, as well as salt substitutes because most substitute potassium for sodium.

Physical Activity and Exercise

Clients with heart failure often experience shortness of breath and fatigue with exercise; however, they should be encouraged to exercise as much as they are able. Many clients with heart failure are not able to fully follow the exercise recommendations of the American Heart Association (see Antihypertensive and Antianginal Drugs), but they can be encouraged to follow an individualized exercise plan. As an alternative, the health care provider may enroll them in cardiac rehabilitation to build their exercise tolerance.

Smoking Cessation and Reducing Alcohol Consumption

Clients should be encouraged to stop using any tobacco products and/or alcohol. Both can cause heart failure exacerbations. For more information on smoking cessation and decreasing alcohol consumption, see Antihypertensive and Antianginal Drugs.

Self-Monitoring of Heart Failure Symptoms

Clients with heart failure should monitor their symptoms daily. This includes weighing themselves every day, monitoring how well they are breathing, assessing for lower extremity swelling, and determining their level of fatigue. Clients should notify their health care provider if they gain 2–3 pounds in one day or 5 pounds in one week or if they notice increased swelling in their extremities, difficulty breathing, and/or chest pain. The American Heart Association website (https://openstax.org/r/heartorgen) (n.d.) has many interactive resources available to help clients monitor their symptoms, including a phone app.

Pharmacologic Treatment of Heart Failure

The primary goal of treatment for clients with heart failure is to reduce morbidity and mortality. Another goal is to decrease the cardiac workload and the heart's demand for oxygen. There are five guideline-directed classifications of medications for HFrEF (Heidenreich et al., 2022):

1. Medications affecting the renin-angiotensin aldosterone system:
    - Angiotensin-converting enzyme inhibitors (ACE inhibitors)
    - Angiotensin receptor blockers (ARBs)
    - Angiotensin receptor/neprilysin inhibitors (ARNIs)
2. Mineralocorticoid receptor agonists (MRAs)
3. Beta-adrenergic blockers (beta blockers)
4. Sodium-glucose cotransport inhibitors (SGLT2Is)
5. Diuretics

ACE inhibitors, ARBs, ARNIs, and MRAs all affect some component of the renin-angiotensin-aldosterone system (RAAS) and are grouped together in Section 19.2. Beta blockers are discussed in Antihypertensive and Antianginal Drugs, but this chapter will highlight the use of them in the management of heart failure. SGLT2Is were primarily used to treat type 2 diabetes but recently were found to be useful in heart failure. Clients with heart failure often have volume overload, so it is also important to control symptoms that are caused by volume overload. Diuretics are part of first-line treatment and are used to modify symptoms of fluid volume overload.

Other drugs are also used in the treatment of heart failure. Adjunct medication therapy will be discussed in Section 19.6.

CLIENT TEACHING GUIDELINES

The client taking a heart failure medication should:

- Take heart failure medications as prescribed by their health care provider.
- Monitor their symptoms of heart failure daily or as directed by their health care provider and keep a record of the symptoms.
- Call their provider if they experience increased ankle swelling, difficulty breathing, and/or chest pain.
- Monitor their weight daily or as directed by the health care provider and keep a record.
- Notify their health care provider if their weight fluctuates 2 pounds in one day or 5 pounds in one week.
- Avoid alcohol, caffeine, and tobacco because these may interfere with the action of cardiovascular drugs.

The client taking heart a failure medication *should not:*

- Take a double dose of the heart failure drug. If the client misses a dose of their drug, they should take it as soon as they remember—unless it's almost time for the next dose. In that case, they should wait and take the next dose at the normal time.
- Abruptly discontinue a heart failure drug without consulting with the health care provider because with some drugs this may cause rebound elevated blood pressure and an elevated pulse rate.
- Take over-the-counter (OTC) drugs and/or herbal supplements without consulting with their health care provider or pharmacist.

Other concerns:

- Heart failure drugs may cause orthostatic hypotension (a form of low blood pressure that occurs when going from a sitting or lying position to a standing position). The client should change positions slowly to prevent dizziness and fainting.
- If low blood pressure develops (feeling dizzy or lightheaded, having blurred vision, feeling weak, or fainting), the client should lie on their back with legs elevated and notify their health care provider.
- If the client is unsure about how to take their heart failure drug, they should call their health care provider or pharmacist.
- If the client is vomiting or otherwise unable to take their medications for more than one day, they should notify their health care provider.

19.2 Drugs Affecting the Renin-Angiotensin-Aldosterone System

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 19.2.1 Identify the characteristics of drugs affecting the renin-angiotensin-aldosterone system that are used to treat heart failure.
- 19.2.2 Explain the indications, actions, adverse reactions, and interactions of drugs affecting the renin-angiotensin-aldosterone system that are used to treat heart failure.
- 19.2.3 Describe nursing implications of drugs affecting the renin-angiotensin-aldosterone system that are used to treat heart failure.
- 19.2.4 Explain the client education related to drugs affecting the renin-angiotensin-aldosterone system that are used to treat heart failure.

Angiotensin-Converting (ACE) Enzyme Inhibitors

As mentioned in Antihypertensive and Antianginal Drugs, **Angiotensin-converting enzyme (ACE) inhibitors** are a classification of drugs that block the body's production of angiotensin II. Angiotensin II is one of the products of the **renin-angiotensin-aldosterone system (RAAS)** (see Figure 19.4), and it stimulates multiple end-organ effects. Two of these effects that are important in heart failure are constriction of arterioles and sodium and water retention of the kidneys. Vasoconstriction causes increased afterload, and sodium and water retention cause increased preload. In heart failure, the heart is already struggling to maintain an adequate cardiac output. Both increased afterload and increased preload will make this task more difficult. ACE inhibitors have been shown to decrease morbidity and

mortality in clients with heart failure (Heidenreich et al., 2022).

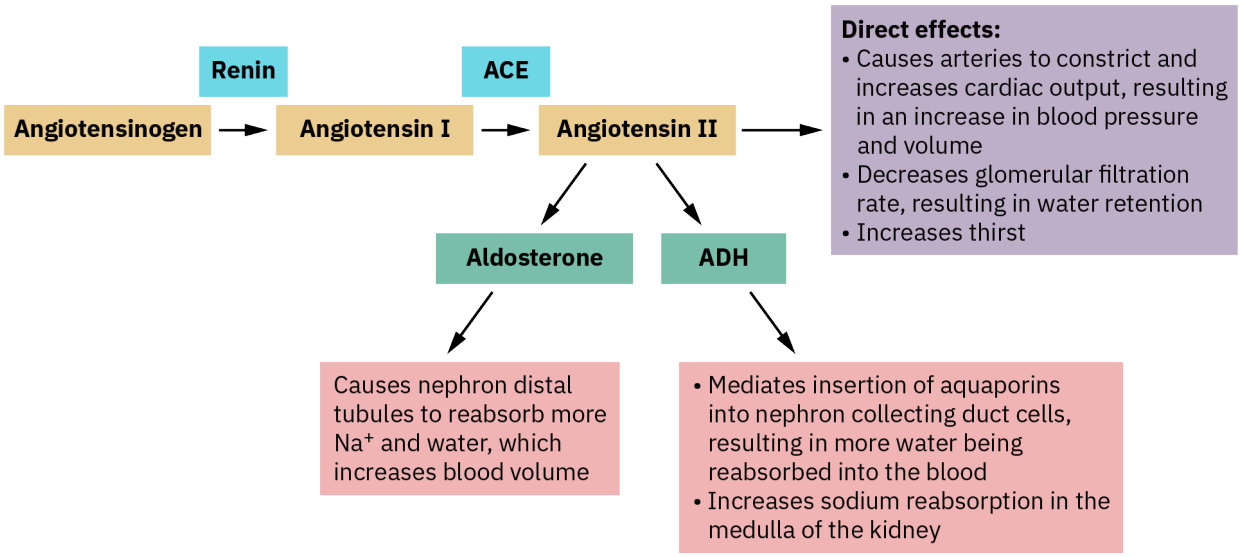


FIGURE 19.4 The renin-angiotensin-aldosterone system produces angiotensin II, which constricts arterioles and increases sodium and water retention in the kidneys. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

ACE inhibitors are used in the management of both hypertension and heart failure. Table 19.3 lists common ACE inhibitors used in the management of heart failure and typical routes and dosing for adult clients. A comprehensive list of ACE inhibitors can be found in Antihypertensive and Antianginal Drugs.

Drug	Routes and Dosage Ranges
Captopril (Capto)	6.25–50 mg orally 3 times daily.
Enalapril (Vasotec)	2.5–20 mg orally twice daily.
Fosinopril (Monopril)	5–40 mg orally daily.
Lisinopril (Zestril)	2.5–40 orally mg daily.
Quinapril (Accupril)	5–20 mg orally twice daily.

TABLE 19.3 Drug Emphasis Table: ACE Inhibitors (source: https://dailymed.nlm.nih.gov/dailymed/)

SPECIAL CONSIDERATIONS

ACE Inhibitors

Black clients with hypertension demonstrate a lower response to ACE inhibitor monotherapy. ACE inhibitors interfere with the renin-angiotensin-aldosterone system, which causes high blood pressure when renin levels are high. Black clients often have hypertension but also have lower levels of renin. Therefore, concomitant therapy may be required to increase response to antihypertensive therapies.

(Source: Astra Zeneca, 2012)

Adverse Effects and Contraindications

ACE inhibitors are relatively safe to use and have a low incidence of serious adverse effects. Adverse effects include angioedema, non-productive cough, neutropenia (low neutrophils in the blood), agranulocytosis (low granulocytes in the blood), proteinuria (protein in the urine), and rash. Hypotension may develop. Clients may develop an ACE inhibitor–associated cough (a persistent, dry, itchy cough). Hyperkalemia (elevated potassium level in the blood)

may develop.

ACE inhibitors cause fetal toxicity and should be immediately discontinued if pregnancy occurs. Clients with renal impairment should use cautiously. Clients with a previous hypersensitivity reaction to an ACE inhibitor should not be prescribed this classification of drug.

Table 19.4 is a drug prototype table for ACE inhibitors featuring lisinopril. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Angiotensin-converting enzyme (ACE) inhibitor **Mechanism of Action** Inhibits the enzyme that converts angiotensin I to angiotensin II and thereby suppresses the renin-angiotensin-aldosterone system	**Drug Dosage** 2.5–40 mg orally twice daily.
Indications Hypertension Heart failure Reduction of mortality in acute myocardial infarction **Therapeutic Effects** Lowers blood pressure Increases blood supply and oxygen to the heart	**Drug Interactions** Aliskiren Lithium Sacubitril **Food Interactions** Alcohol Tobacco
Adverse Effects Angioedema Hyperkalemia Fatigue Orthostatic hypotension Asthenia Diarrhea Nausea/vomiting Headache Dizziness/vertigo Cough Rash Abdominal pain Angina	**Contraindications** Hypersensitivity History of angioedema Pregnancy (fetal toxicity) Caution: Aortic stenosis Diabetes Syncope Orthostatic hypotension Impaired renal function Breastfeeding

TABLE 19.4 Drug Prototype Table: Lisinopril (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ACE inhibitors:

- Assess the client's blood pressure and pulse on an ongoing basis with initial dosing and intermittently during drug therapy.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

SAFETY ALERT

ACE Inhibitors

Taking ACE inhibitors with potassium-containing salt substitutes or consuming large amounts of high-potassium foods increases the risk of hyperkalemia. Having a blood potassium level above 6.0 mmol/L is considered a medical emergency and can result in cardiac arrest.

Clients of childbearing age should take measures not to become pregnant while taking ivabradine due to teratogenic effects (causing harm to embryo or fetus).

CLIENT TEACHING GUIDELINES

The client taking an ACE inhibitor should:

- Avoid foods high in potassium and salt substitutes (because these are high in potassium) due to the aldosterone release.
- Report side effects such as cough, angioedema, or anaphylactic reactions to their health care provider.
- Notify their health care provider if they experience abdominal pain, joint or muscle aches, muscle weakness, change in the amount of urine produced, or trouble breathing.
- Be aware that a persistent cough may develop when taking ACE inhibitors.
- Notify their health care provider if pregnant, planning on getting pregnant, or breastfeeding prior to starting an ACE inhibitor.
- Report symptoms such as chest pain, slurred speech, hemiparesis, and difficulty speaking or walking to their health care provider immediately because these may be symptoms of a heart attack or stroke.
- Notify their health care provider about symptoms such as dizziness, lightheadedness, or fainting because these could be related to low blood pressure.

Angiotensin II Receptor Blockers

Angiotensin II receptor blockers (ARBs) are a classification of drugs that bind to and inhibit angiotensin II type I receptors. ARBs work directly at the receptor site to block angiotensin II from binding with receptors on the cells (see Figure 19.4). The effect of ARBs is similar to that of ACE inhibitors; however, the side effects are lessened. This means that the potential for angioedema is decreased. Also, there is no side effect of cough.

Angiotensin II receptor blockers decrease blood pressure and therefore decrease afterload. This is beneficial in treating heart failure since decreased afterload means the heart does not have to work as hard to generate stroke volume.

Table 19.5 lists common ARBs used in the management of heart failure and typical routes and dosing for adult clients. A comprehensive list of ARBs can be found in Antihypertensive and Antianginal Drugs.

Drug	Routes and Dosage Ranges
Candesartan (Atacand)	4 mg orally daily; maximum dose: 32 mg daily.
Losartan (Cozaar)	25–150 orally mg daily.
Valsartan (Diovan)	20–160 orally mg daily.

TABLE 19.5 **Drug Emphasis Table: ARBs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of ARBs include dizziness, muscle cramps, weakness, heartburn, diarrhea, leg swelling, headaches, and weight loss. Serious adverse effects include angioedema, hypotension, hepatic impairment, and hyperkalemia.

ARBs cause fetal toxicity and should not be taken during pregnancy. Clients with hepatic impairment should use ARBs cautiously. Clients with a previous hypersensitivity reaction or angioedema to an ARB inhibitor should not be prescribed this classification of drug. Clients with a history of mood disturbances or who are at risk for mood disturbances should be monitored closely for suicidal ideation.

Table 19.6 is a drug prototype table for ARBs featuring losartan. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Angiotensin II receptor blocker (ARB) **Mechanism of Action** Blocks the binding of angiotensin II to the angiotensin I receptor, thereby decreasing vasoconstriction and lowering blood pressure	**Drug Dosage** 25–150 mg orally daily.
Indications Hypertension Heart failure Nephropathy in clients with type 2 diabetes **Therapeutic Effects** Lowers blood pressure Increases blood supply and oxygen to the heart	**Drug Interactions** Aliskiren Lithium Potassium-sparing diuretics (may increase hyperkalemia) **Food Interactions** Alcohol Tobacco
Adverse Effects Hyperkalemia Dizziness Syncope Increased thirst Decreased urinary output Irregular heartbeat Angioedema	**Contraindications** Hypersensitivity Pregnancy (fetal toxicity) Caution: Hepatic impairment Renal impairment Hypotension Hypovolemia Hyperkalemia

TABLE 19.6 **Drug Prototype Table: Losartan** (source: https://dailymed.nlm.nih.gov/dailymed/)

SPECIAL CONSIDERATIONS

ARBs

The RAAS has been associated with increased risk of mood disorders. The use of ARBs may be associated with an increased risk of suicide compared with other antihypertensive therapies.

Black clients with hypertension demonstrate a lower response to ARB monotherapy. Concomitant therapy may be required to increase response to antihypertensive therapies.

Older adults and clients with hepatic impairment should start on a low initial dose because the drug is metabolized by the liver.

(Source: Colvin et al., 2020)

Nursing Implications

The nurse should do the following for clients who are taking ARBs:

- Monitor the client's blood pressure as prescribed.
- Monitor the client for interactions because many medications and herbal supplements interact with ARBs.
- Monitor the client for adverse effects, including electrolyte imbalances and alterations in liver and renal function.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ARB should:

- Avoid foods high in potassium and salt substitutes (because these substitute potassium for sodium) due to the aldosterone release.
- Report side effects such as cough, angioedema, or anaphylactic reactions to the health care provider.
- Notify their health care provider if they experience abdominal pain, joint or muscle aches, muscle weakness, change in the amount of urine produced, or trouble breathing.
- Notify their health care provider if pregnant, planning on getting pregnant, or breastfeeding prior to starting an ARB.
- Notify their health care provider about symptoms such as dizziness, lightheadedness, or fainting because these could be related to low blood pressure.

Angiotensin Receptor/Neprilysin Inhibitors

Recently, a new classification of heart failure medication was developed, **angiotensin receptor/neprilysin inhibitors (ARNIs)**. This combination medication is a first-line medication for many classifications of heart failure. It is a combination of an ARB and a new type of medication, a neprilysin inhibitor. There currently is only one medication in the ARNI class: sacubitril/valsartan (Entresto).

In heart failure with reduced ejection fraction, there is a lot of stress on the left ventricle as well as left ventricular dilation. This is due to an increased preload. When the ventricle dilates to a point that is no longer helpful to the heart, the myocytes release brain natriuretic peptide (BNP). BNP stimulates a compensatory mechanism that leads to vasodilation and decreased sodium and water absorption. Vasodilation and diuresis decrease afterload and preload, which makes the workload of the heart decrease.

Neprilysin is an enzyme that breaks down BNP. The inhibition of neprilysin means that BNP can stay in the body's circulatory system longer. If BNP stays in the system longer, then vasodilation and decreased sodium and water reabsorption will last longer, which will decrease afterload and preload. This will decrease the workload of the heart.

Adverse Effects and Contraindications

Adverse effects of ARNIs include angioedema, hypotension, renal impairment, and hyperkalemia.

ARNIs contain ARBs and cause fetal toxicity; they should not be taken during pregnancy. Clients with hepatic impairment should use ARNIs cautiously. Clients with a previous hypersensitivity or angioedema reaction to an ARB inhibitor should not be prescribed this classification of drug. Clients with a history of mood disturbances or who are at risk for mood disturbances should be monitored closely for suicidal ideation.

CLINICAL TIP

Reviewing Medications

It is important for the nurse to review all of a client's medications. Clients should not take ACE inhibitors, ARBs, or ARNIs at the same time. Clients should be prescribed only one of these classifications of medication at a time.

Table 19.7 is a drug prototype table for angiotensin receptor/neprilysin inhibitors featuring sacubitril/valsartan. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Angiotensin receptor/neprilysin inhibitor **Mechanism of Action** Causes angiotensin receptor blockade and inhibition of the enzyme that breaks down BNP	**Drug Dosage** Initial dose: 49 mg/51 mg orally twice daily; maximum dose: 97 mg/103 mg twice daily.
Indications Heart failure **Therapeutic Effects** Vasodilation	**Drug Interactions** Potassium-sparing diuretics (may lead to increased serum potassium) Nonsteroidal anti-inflammatory drugs (NSAIDs; may lead to increased risk of renal impairment) Lithium (increased risk of lithium toxicity) ACE inhibitors (increased risk of angioedema) **Food Interactions** No significant interactions
Adverse Effects Angioedema Hypotension Hyperkalemia Cough Dizziness Renal failure	**Contraindications** Pregnancy (fetal toxicity) History of angioedema with ACE inhibitor or ARB therapy

TABLE 19.7 **Drug Prototype Table: Sacubitril/Valsartan** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ARNIs:

- Monitor the client's blood pressure as prescribed.
- Monitor the client for medication and herbal supplement interactions.
- Report adverse effects, including electrolyte imbalances and alterations in liver and renal function, to the health care provider.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ARNI should:

- Avoid foods high in potassium and salt substitutes (because these are high in potassium) due to the aldosterone release.
- Report side effects such as cough, angioedema, and anaphylactic reactions to the health care provider.
- Notify their health care provider if they experience abdominal pain, joint or muscle aches, muscle weakness, change in the amount of urine produced, or trouble breathing.
- Notify their health care provider if pregnant, planning on getting pregnant, or breastfeeding prior to starting an ARNI.
- Notify their health care provider about symptoms such as dizziness, lightheadedness, or fainting because these could be related to low blood pressure.

Mineralocorticoid Receptor Antagonists

Mineralocorticoid receptor antagonists (MRAs) (also known as aldosterone antagonists) are often categorized as diuretics because they ultimately do cause diuresis. When the RAAS is activated, one of the end results is the stimulation of the adrenal glands to secrete aldosterone. (See Figure 19.4 earlier in the chapter.) Aldosterone binds

to receptors on cells in the distal tubule of the nephron, which then causes them to reabsorb sodium and water. During this process, potassium secretion increases. Aldosterone antagonists block the receptor so that aldosterone can't bind there. The end result is increased sodium and water excretion into the urine, and potassium reabsorption. Aldosterone antagonists are referred to as potassium-sparing diuretics.

MRA medications have been found to reduce the risk of all-cause mortality in clients with heart failure (Heidenreich et al., 2022).

Table 19.8 lists the two MRAs used in heart failure and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Spironolactone (Aldactone)	12.5–25 mg orally daily; maximum dose: 50 mg daily.
Eplerenone (Inspra)	25–50 mg orally daily.

TABLE 19.8 **Drug Emphasis Table: MRAs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of MRAs include hyperkalemia, hypotension, worsening renal failure, electrolyte abnormalities, and gynecomastia (breast enlargement and/or sensitivity).

MRAs should not be taken during pregnancy. Because MRAs cause potassium retention, they should not be used by clients who have kidney disease. MRAs must be used carefully with other medications, such as ACE inhibitors and ARBs, that may cause hyperkalemia.

Table 19.9 is a drug prototype table for MRAs featuring spironolactone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Mineralocorticoid receptor antagonist (MRA) **Mechanism of Action** Binds to receptors in the nephron so that aldosterone is not able to bind, which leads to increased diuresis	**Drug Dosage** 12.5–25 mg orally daily; maximum dose: 50 mg daily.
Indications Heart failure Hypertension Edema associated with hepatic cirrhosis or nephrotic syndrome **Therapeutic Effects** Diuresis	**Drug Interactions** Agents that increase serum potassium Lithium (increased risk for lithium toxicity) NSAIDs Digoxin Aspirin (may reduce the efficacy of spironolactone) **Food Interactions** No significant interactions
Adverse Effects Hyperkalemia Hypotension Worsening renal failure Electrolyte abnormalities Gynecomastia	**Contraindications** Hyperkalemia Addison's disease Pregnancy Concomitant use of eplerenone

TABLE 19.9 **Drug Prototype Table: Spironolactone** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

MRAs

MRAs can cause significant hyperkalemia. The client should have their serum electrolytes monitored regularly while taking MRAs. If hyperkalemia occurs, the drug may have to be discontinued.

Nursing Implications

The nurse should do the following for clients who are taking MRAs:

- Monitor the client for medication and/or food interactions.
- Monitor the client for adverse effects, including electrolyte imbalances and alteration renal function.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an MRA should:

- Avoid foods high in potassium and salt substitutes (because these are high in potassium) due to the aldosterone release.
- Notify their provider if they are taking an ACE inhibitor, ARB, or other potassium-sparing drugs.
- Notify their health care provider if pregnant, planning on getting pregnant, or breastfeeding prior to starting an MRA.
- Notify their health care provider about breast enlargement and/or tenderness.
- Notify their health care provider about symptoms such as dizziness, lightheadedness, or fainting because these could be related to low blood pressure.

FDA BLACK BOX WARNING

Drugs Affecting the Renin-Angiotensin-Aldosterone System

Fetal toxicity can occur when taking **ACE inhibitors** during the second and third trimesters of pregnancy or when taking **ARBs** or **ARNIs** during pregnancy.

19.3 Beta-Adrenergic Blockers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 19.3.1 Identify the characteristics of beta-adrenergic blocker drugs used to treat heart failure.
- 19.3.2 Explain the indications, actions, adverse reactions, and interactions of beta-adrenergic blocker drugs used to treat heart failure.
- 19.3.3 Describe nursing implications of beta-adrenergic blocker drugs used to treat heart failure.
- 19.3.4 Explain the client education related to beta-adrenergic blocker drugs used to treat heart failure.

As presented in Antihypertensive and Antianginal Drugs, **beta-adrenergic blockers** (beta blockers) are a classification of drugs that inhibit chronotropic, inotropic, and vasoconstrictor response to catecholamine, epinephrine, and norepinephrine. They do this by exerting effects on adrenergic receptors beta 1, beta 2, and alpha.

When the body is presented with a stressor, the sympathetic nervous system is activated. Catecholamines (norepinephrine and epinephrine) are released with the primary purpose of enhancing the fight-or-flight response. Catecholamines interact with beta-1, beta-2, and alpha receptors. Beta-1 receptors are found in the heart and kidneys, beta-2 receptors are found in cardiac tissue, and alpha receptors are found on arteries and veins.

Beta blockers can inhibit catecholamines from binding to beta-1, beta-2, and/or alpha receptors. This means that

the sympathetic response (or the fight-or-flight response) is decreased. Part of the sympathetic response is to increase heart rate and contractility, increase blood pressure, and dilate bronchioles so that the body can run away or fight the threat. In general, beta blockers decrease heart rate and contractility, decrease blood pressure, and may cause some bronchoconstriction.

Select beta blockers have been found to decrease mortality in clients with heart failure (Heidenreich et al., 2022). Metoprolol and bisoprolol are two cardio-selective beta blockers, and carvedilol is a nonselective beta blocker that is used in the management of clients with heart failure.

Cardio-selective beta blockers affect the heart by reducing heart rate and contractility. Nonselective beta blockers affect the heart in the same way, but they also cause vasodilation due to their effects on alpha receptors of the arteries.

In heart failure, either cardio-selective beta blockers (bisoprolol, metoprolol succinate) or nonselective beta blockers (carvedilol) are used to decrease heart rate and contractility. Nonselective beta blockers also decrease blood pressure, which decreases afterload. If the heart rate is decreased, there is more time for diastole, or ventricular filling. Recall that coronary arteries deliver blood to the cardiac myocytes of the ventricles during diastole. This means that the ventricles themselves are getting more oxygen-rich blood. Also, if contractility is decreased, there is less demand for oxygen. Nonselective beta blockers also decrease afterload, which means the heart does not have to produce as much force to generate stroke volume.

Beta blockers are used to treat clients with hypertension, heart failure, arrhythmias, myocardial infarctions, migraines, glaucoma, and certain types of tremors. Beta blockers have also been used by health care providers as anxiolytics (to reduce anxiety).

Table 19.10 lists the beta blockers that are commonly used for heart failure and typical routes and dosing for adult clients. A complete list of beta blockers can be found in Antihypertensive and Antianginal Drugs.

Drug	Routes and Dosage Ranges
Bisoprolol (Zebeta)	1.25–10 mg orally once daily.
Carvedilol (Coreg)	3.125–50 mg orally daily; maximum dose: 50 mg twice daily.
Metoprolol succinate (Toprol XL)	12.5–200 mg orally daily; maximum dose: 200 mg daily.

TABLE 19.10 Drug Emphasis Table: Beta Blockers (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of beta blockers include dizziness, fatigue, weight gain, constipation, cold hands and feet, hypercholesterolemia, shortness of breath, depression, nausea, dry mouth, and dry eyes. Serious adverse effects include bradycardia, arrhythmias, hypoglycemia, and hypotension. Rare side effects include sexual and erectile dysfunction.

Blood pressure and pulse rate should be monitored prior to administration. Beta blockers should not be administered if the client is hypotensive or has a heart rate less than 50–60 beats per minute, or as directed by the health care provider.

Nonselective beta blockers are contraindicated in clients with moderate to severe asthma and/or chronic lung diseases due to the potential for causing an exacerbation. Beta blockers should be used cautiously in clients with AV node and sinus bradycardia because they can aggravate these conditions. Beta blockers may exacerbate symptoms of Raynaud's phenomenon or cause this disease process in clients. Clients with diabetes should use beta blockers cautiously because they can mask the symptoms of hypoglycemia, causing confusion, fainting, or seizures.

SAFETY ALERT

Beta Blockers

Nonselective beta blockers should not be used in clients with asthma who are taking a short-acting beta agonist because they may cause worsening bronchospasm.

Beta blockers block aspects of the sympathetic nervous system, which is activated when blood sugar is too low. Beta blockers may mask symptoms of hypoglycemia.

Table 19.11 is a drug prototype table for beta blockers featuring metoprolol succinate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Beta-adrenergic blocker **Mechanism of Action** Blocks beta-1 receptors, thereby decreasing cardiac workload by slowing the heart and decreasing the systolic blood pressure	**Drug Dosage** 12.5–200 mg orally daily; maximum dose: 200 mg daily.
Indications Hypertension Heart failure Angina **Therapeutic Effects** Lowers blood pressure Decreases cardiac workload	**Drug Interactions** Albuterol Clonidine Fluoxetine Mefloquine Paroxetine Propafenone Quinidine **Food Interactions** Caffeine Alcohol Tobacco
Adverse Effects Hypotension Bradycardia Fatigue/weakness Dizziness Headache Blurred vision Dry mouth Nausea/vomiting/diarrhea Drowsiness/insomnia Tinnitus Peripheral edema Erectile dysfunction	**Contraindications** Hypersensitivity AV block Sick sinus syndrome Cardiogenic shock Acute decompensated heart failure Severe bradycardia Caution: Thyroid impairment Hepatic impairment Asthma Peripheral vascular disease Diabetes mellitus Chronic obstructive pulmonary disease (COPD) Cerebrovascular disease

TABLE 19.11 **Drug Prototype Table: Metoprolol Succinate** (source: https://dailymed.nlm.nih.gov/dailymed/)

CLINICAL TIP

Assessing Comorbidities

As a nurse, it is important to assess a client's comorbidities prior to administering drugs. When administering beta blockers, the nurse should assess whether the client has asthma or chronic obstructive pulmonary disease and is taking a short-acting beta agonist because this may cause a pharmacodynamics drug interaction.

Nursing Implications

The nurse should do the following for clients who are taking beta-adrenergic blockers:

- Assess the client's blood pressure and pulse on an ongoing basis with initial dosing and intermittently during drug therapy. The beta-adrenergic blocker should be withheld if the client's heart rate is less than 50–60 beats/minute or as directed by the health care provider.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a beta-adrenergic blocker should:

- Take their pulse as directed prior to taking a beta-adrenergic blocker and do not administer the drug if the pulse is less than 50–60 beats/minute or as directed by their health care provider.
- Take this medication without regard to meals.
- Report side effects such as bradycardia, hypotension, fatigue, dizziness, constipation, or sexual dysfunction to their health care provider.
- Monitor for symptoms of worsening heart failure such as fatigue, weight gain, and peripheral edema.
- Monitor blood glucose levels closely because beta blockers can mask symptoms of hypoglycemia.
- Notify their health care provider about symptoms such as dizziness, lightheadedness, or fainting because these could be related to low blood pressure and/or low heart rate.

The client taking a beta-adrenergic blocker *should not:*

- Take beta-adrenergic blockers with OTC drugs or herbal supplements, such as ma-huang, ephedra, black cohosh, hawthorne, or licorice, without consulting their health care provider because these supplements may interfere with the action of the beta-adrenergic blocker.

FDA BLACK BOX WARNING

Beta-Adrenergic Blockers

Beta blocker therapy should not be abruptly stopped, but gradually tapered to avoid exacerbation of angina and myocardial infarction. Clients should seek health care provider advice prior to discontinuing use.

19.4 Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2Is)

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 19.4.1 Identify the characteristics of sodium-glucose cotransporter 2 inhibitor drugs used to treat heart failure.
- 19.4.2 Explain the indications, actions, adverse reactions, and interactions of the sodium-glucose cotransporter 2 inhibitor drugs used to treat heart failure.
- 19.4.3 Describe nursing implications of sodium-glucose cotransporter 2 inhibitor drugs used to treat heart failure.
- 19.4.4 Explain the client education related to sodium-glucose cotransporter 2 inhibitor drugs used to treat heart failure.

Initially, **sodium-glucose cotransporter 2 inhibitor (SGLT2I)** medications were introduced as pharmacologic therapy for clients with type 2 diabetes. After years of use in clients with type 2 diabetes and comorbid heart failure, the benefits of SGLT2Is were noted and researched for all clients with heart failure (regardless of whether they also had type 2 diabetes). Subsequently, SGLT2Is were found to reduce mortality in clients with heart failure, and a new class of medications for heart failure was introduced (Heidenreich et al., 2022).

The nephrons in the kidneys actively reabsorb glucose. Nearly all glucose is reabsorbed in the proximal tubule by "piggybacking" it with sodium reabsorption. Sodium is actively reabsorbed (requires energy expenditure), and during the process, glucose is also reabsorbed via a cotransporter system. If the cotransporter is inhibited, then less sodium and glucose are reabsorbed. That means that more sodium and glucose will pass through the nephron into the collecting duct and ultimately into the urine. Since sodium and glucose are solutes, or osmotically active, more water will also end up in the urine, which will result in diuresis.

The diuretic effect of SGLT2Is helps to reduce preload. If preload is reduced, then the heart does not have to work as hard. There also appear to be direct benefits that help the left ventricle pump more effectively, which is most likely the reason these drugs have become first-line therapy for clients with heart failure (Shah & Fang, 2022).

Table 19.12 lists the two SGLT2Is that are FDA-approved for heart failure and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Dapagliflozin (Farxiga)	10 mg orally daily; maximum dose: 10 mg orally daily.
Empagliflozin (Jardiance)	10 mg orally daily; maximum dose: 10 mg orally daily.

TABLE 19.12 Drug Emphasis Table: SGLT2Is (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of SGLT2Is include ketoacidosis in clients with diabetes mellitus, urinary tract infection, pyelonephritis, genital infection, necrotizing fasciitis of the perineum, volume depletion, and hypotension.

Contraindications to SGLT2Is include history of serious hypersensitivity reaction to dapagliflozin, chronic and/or acute kidney disease, and pregnancy.

Table 19.13 is a drug prototype table for SGLT2Is featuring dapagliflozin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Sodium-glucose cotransporter 2 inhibitor **Mechanism of Action** Blocks reabsorption of sodium and glucose in the proximal tubule by inhibiting the sodium-glucose cotransporter	**Drug Dosage** 10 mg orally daily; maximum dose: 10 mg orally daily.
Indications Heart failure Diabetes type 2 **Therapeutic Effects** Diuresis Reduced blood glucose	**Drug Interactions** Insulin (hypoglycemia) Lithium **Food Interactions** No significant interactions
Adverse Effects Ketoacidosis in clients with diabetes mellitus Volume depletion/hypotension Urinary tract infection Pyelonephritis Genital infection Necrotizing fasciitis of the perineum Hypoglycemia	**Contraindications** History of serious hypersensitivity reaction to dapagliflozin Severe renal impairment, end-stage renal disease, or dialysis Pregnancy (potential fetal risk in third trimester)

TABLE 19.13 **Drug Prototype Table: Dapagliflozin** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

SGLT2Is

Clients must be assessed for volume status prior to initiating an SGLT2I. When administering SGLT2Is, it is important to assess whether the client has signs of dehydration such as sunken eyes, skin tenting, or rapid heart rate. The nurse should notify the provider if these signs are noted prior to administering an SGLT2I. Low fluid volume can lead to significant hypotension with this drug.

Clients' renal status also must be assessed prior to initiating SGLT2Is.

Nursing Implications

The nurse should do the following for clients who are taking SGLT2Is:

- Assess the client's blood pressure and pulse on an ongoing basis with initial dosing and intermittently during drug therapy.
- Monitor the client for interactions because many medications and herbal supplements interact with SGLT2Is.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an SGLT2I should:

- Inform their health care provider if they have diabetes and take insulin. Both insulin and SGLT2Is lower blood glucose. The client may be prescribed a lower dose of either of the two drugs.
- Inform their health care provider if they have been told they have renal insufficiency.
- Monitor for signs and symptoms of dehydration such as dry mouth or lightheadedness. SGLT2Is can cause

significant hypotension in the presence of hypovolemia.
- Inform their health care provider if they are pregnant or intend to become pregnant.

19.5 Diuretics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 19.5.1 Identify the characteristics of the diuretic drugs used to treat heart failure.
- 19.5.2 Explain the indications, actions, adverse reactions, and interactions of the diuretic drugs used to treat heart failure.
- 19.5.3 Describe nursing implications of diuretic drugs used to treat heart failure.
- 19.5.4 Explain the client education plan related to diuretic drugs used to treat heart failure.

Diuretics were introduced in Antihypertensive and Antianginal Drugs. This chapter discusses diuretics that are used in heart failure, specifically loop diuretics and thiazide and thiazide-like diuretics. Typically, potassium-sparing diuretics, except for mineralocorticoid receptor agonists, are used sparingly in the treatment of heart failure because the combination of ACE inhibitor or ARB with a potassium-sparing diuretic can lead to increased potassium levels.

Loop Diuretics

Loop diuretics block the reabsorption of sodium and chloride in the loop of Henle, which is located in the renal tubule. Due to the way the sodium pump works, loop diuretics also block the reabsorption of potassium. Loop diuretics in general are more potent than thiazide diuretics since the majority of sodium and chloride reabsorption occurs in the loop of Henle. Loop diuretics are often the first choice of diuretics in treating heart failure.

CLINICAL TIP

Potassium Supplements

Clients should be informed they may have to take prescribed potassium supplements when taking loop diuretics.

SAFETY ALERT

Diuretics

Loop diuretics are potent diuretics that can lead to profound dehydration and electrolyte loss.

Thiazide and Thiazide-Like Diuretics

As discussed in Antihypertensive and Antianginal Drugs, thiazide and thiazide-like diuretics block the reabsorption of sodium and chloride in the distal renal tubule. Due to the nature of sodium reabsorption, thiazide and thiazide-like diuretics cause potassium loss as well as sodium loss.

Table 19.14 lists common loop diuretics and thiazide/thiazide-like diuretics used in heart failure and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Bumetanide (Bumex)	*Heart failure:* *Oral:* 0.5–2 mg twice daily; maximum dose: 10 mg daily. *Intramuscular/intravenous (IV):* 0.5–1 mg every 2–3 hours; maximum dose: 10 mg daily.
Furosemide (Lasix)	*Edema:* 20–80 mg orally twice daily; maximum dose: 600 mg daily. (Doses exceeding 80 mg daily must be monitored carefully with frequent follow-up and laboratory monitoring.)

TABLE 19.14 **Drug Emphasis Table: Diuretics Used in Heart Failure** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Torsemide (Demadex)	*Heart failure*: 10–20 mg orally daily, titrated; maximum dose: 200 mg daily.
Chlorothiazide (Diuril)	*Edema:* 250–500 mg IV once or twice daily; maximum dose: 1000 mg daily.
Chlorthalidone (Thalitone)	*Edema:* 50–100 mg orally daily or 100 mg every other day; maximum dose: 200 mg daily.
Hydrochlorothiazide (Microzide, HCTZ)	*Edema:* 25–100 mg orally daily.
Indapamide (Lozol)	*Edema:* 2.5 mg orally daily; maximum dose: 5 mg daily.
Metolazone (Zaroxolyn)	*Edema or heart failure:* 5–20 mg orally once daily.

TABLE 19.14 Drug Emphasis Table: Diuretics Used in Heart Failure (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects include severe anaphylactic/anaphylactoid reaction, excessive loss of water and electrolytes, ototoxicity, tinnitus and hearing loss, vertigo, dizziness, aplastic anemia, thrombocytopenia, agranulocytosis, hemolytic anemia, leukopenia, anemia, Stevens-Johnson syndrome, drug rash, and cramping/diarrhea.

Clients with hypersensitivity to diuretics should not take this classification of drugs. All diuretics should be used with caution in older clients and/or clients with hepatic or renal impairment, arrhythmias, or gout.

Table 19.15 is a drug prototype table for diuretics featuring furosemide (a loop diuretic). It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications. (Hydrochlorothiazide, a thiazide/thiazide-like diuretic, was featured in Antihypertensive and Antianginal Drugs.)

Drug Class Loop diuretic **Mechanism of Action** Blocks the reabsorption of sodium in the loop of Henle, which causes sodium and water to be excreted	**Drug Dosage** *Edema:* 20–80 mg orally twice daily; maximum dose: 600 mg daily. (Doses exceeding 80 mg daily must be monitored carefully with frequent follow-up and laboratory monitoring.)
Indications Hypertension Congestion and/or edema in heart failure **Therapeutic Effects** Lowers blood pressure Decreases edema	**Drug Interactions** Aminoglycoside (may increase risk of ototoxicity) **Food Interactions** No significant interactions
Adverse Effects Severe anaphylactic/anaphylactoid reaction Orthostatic hypotension Excessive loss of water and electrolytes Ototoxicity Tinnitus and hearing loss Vertigo Dizziness Aplastic anemia Thrombocytopenia Agranulocytosis Hemolytic anemia Leukopenia Anemia Stevens-Johnson syndrome Drug rash Cramping/diarrhea	**Contraindications** Allergy to furosemide Anuria Caution: Hepatic disease Renal disease

TABLE 19.15 **Drug Prototype Table: Furosemide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking diuretics:

- Assess the client's blood pressure and pulse on an ongoing basis with initial dosing and intermittently during drug therapy.
- Assess the client for electrolyte imbalances and hyperglycemia as well as the client's urine output. Urine output should be at least 30 mL/hour or 600 mL/24 hours.
- Assess and monitor for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking any type of diuretic should:

- Take diuretic as prescribed by the health care provider.
- Take diuretic earlier in the day (morning) so that diuresis occurs before sleeping times.
- Report a weight loss or weight gain greater than 2 pounds a day or 5 pounds a week to the health care provider.
- Notify their health care provider about symptoms such as dizziness, lightheadedness, or fainting because these could be related to low blood pressure.

The client taking a loop diuretic should:

- Report adverse effects such as dizziness or lightheadedness, fatigue, increased bleeding, tinnitus, weakness, and leg cramps to the provider.
- Eat potassium-rich foods to replace potassium.

FDA BLACK BOX WARNING

Diuretics

Loop diuretics are a potent diuretic and could lead to diuresis with water and electrolyte depletion.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Anna Rodriguez is an 85-year-old client who presents to her health care provider with an exacerbation of heart failure. Anna reports increasing shortness of breath with self-care activities. She also shares that she is no longer going to the senior center because getting in and out of the car leaves her short of breath and fatigued. She also reports that her feet feel "heavy" and that she has gained 3 pounds in the last 1–2 weeks. Anna sleeps on two pillows and does not awaken during the night with shortness of breath. She has also had a persistent itchy, dry cough and asks if she has a respiratory infection. The cough is nonproductive, and Anna reports no fever, chills, achy feeling, congestion, or chest pain.

Anna reports following a low-sodium diet and does not engage in exercise. She is a nonsmoker and does not drink alcohol.

History
Heart failure with preserved ejection fraction
Hypothyroidism

Current Medications
Lisinopril 10 mg twice daily
Levothyroxine 50 mcg once daily

Vital Signs		Physical Examination
Temperature:	98.2°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Neurological:* Within normal limits • *Cardiovascular:* No jugular venous distension, 1+ pitting edema of feet and ankles. S1 and S2 heard on heart auscultation. No S3 noted. Brisk capillary refill in nailbeds of hands and feet. • *Respiratory:* Crackles auscultated in lung bases bilaterally • *Gastrointestinal:* Abdominal sounds heard in all four quadrants, no tenderness, no distension • *Integumentary:* Skin appropriate for age
Heart rate:	95 beats/min	
Respiratory rate:	22 breaths/min	
Blood pressure:	158/94 mm Hg	
Height:	5'4"	
Weight:	152 lb (up 7 lb per client)	

TABLE 19.16

1. The nurse is reviewing enalapril administration with Anna. Which instruction about this drug will the nurse provide?
    a. Avoid green, leafy vegetables.
    b. Do not take if your heart rate is less than 60 beats/minute.
    c. Avoid salt substitutes that contain potassium.
    d. Report feelings of depression.

2. The nurse notes that Anna has 1+ pitting edema in the feet and ankles, a recent weight gain, and crackles in her lung bases. The nurse anticipates that the provider will order which drug?
    a. Digoxin
    b. Furosemide
    c. Hydralazine/isosorbide dinitrate
    d. Valsartan

19.6 Adjunct Medications Used in Heart Failure

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 19.6.1 Identify the characteristics of adjunct medications used to treat heart failure.
- 19.6.2 Explain the indications, actions, adverse reactions, and interactions of adjunct medications used to treat heart failure.
- 19.6.3 Describe nursing implications of adjunct medications used to treat heart failure.
- 19.6.4 Explain the client education related to adjunct medications used to treat heart failure.

Hydralazine and Isosorbide Dinitrate

Hydralazine and isosorbide dinitrate (BiDil) are administered as a combination drug in clients with heart failure who have optimized therapy with other medications but still have a low ejection fraction and/or symptoms. This drug combination has been shown to reduce mortality in Black clients with heart failure (Heidenreich et al., 2022). Research has not shown a decreased mortality in clients with heart failure who are not Black, but there may be some benefit to adding hydralazine and isosorbide dinitrate or to using this therapy if clients are not able to tolerate first-line therapy.

The combination of hydralazine and isosorbide dinitrate causes vasodilation, which decreases afterload, or the amount of force that the heart must pump against. Hydralazine directly vasodilates arterioles. Although the mechanism of action is not well understood, it is thought to decrease calcium release in the smooth muscles around arterioles. Because calcium is an essential component of muscle contraction, if less calcium is available, then the smooth muscle will contract less and the arteriole will not be constricted.

Isosorbide dinitrate is a part of the nitrate drug classification that was discussed in Antihypertensive and Antianginal Drugs. Nitrates cause the release of nitric oxide within the endothelium of blood vessels. Nitric oxide causes a series of events that ultimately lead to vasodilation.

Adverse Effects and Contraindications

Adverse effects include orthostatic hypotension, tachycardia, paradoxical bradycardia, flushing, peripheral edema, nausea/vomiting, headache (nitrates), blurred vision, drug-induced lupus erythematosus, hemolytic anemia, and glomerulonephritis.

Contraindications include allergy to nitrates and use with phosphodiesterase type 5 (PDE5) inhibitors.

Table 19.17 is a drug prototype table featuring hydralazine and isosorbide dinitrate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Arteriolar vasodilator/nitrate vasodilator **Mechanism of Action** Hydralazine directly vasodilates arterioles by causing smooth muscle relaxation. Isosorbide dinitrate causes the release of nitric oxide, which ultimately leads to vasodilation.	**Drug Dosage** *Heart failure:* 20 mg isosorbide dinitrate with 37.5 mg hydralazine orally 3 times daily; maximum dose: 40 mg isosorbide dinitrate with 75 mg hydralazine orally 3 times daily.
Indications Adjunct treatment to standard therapy for self-identified Black clients with heart failure and/or clients who are not able to tolerate standard therapy **Therapeutic Effects** Lowers blood pressure, which decreases afterload	**Drug Interactions** Phosphodiesterase type 5 (PDE5) inhibitors **Food Interactions** No significant interactions
Adverse Effects Orthostatic hypotension Dizziness Tachycardia Paradoxical bradycardia Flushing Peripheral edema Nausea/vomiting Headache (nitrates) Blurred vision Drug-induced lupus erythematosus Hemolytic anemia Glomerulonephritis	**Contraindications** PDE5 inhibitors Allergy to nitrates

TABLE 19.17 **Drug Prototype Table: Hydralazine/Isosorbide Dinitrate** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Hydralazine

Nitrates can cause hypotension; nitrates in combination with hydralazine can cause significant hypotension. This medication should not be taken with PDE5 inhibitors because this can lead to profound hypotension.

Nursing Implications

The nurse should do the following for clients who are taking hydralazine/isosorbide dinitrate:

- Assess the client's drug and herbal supplements because significant hypotension may occur when used in conjunction with nitrates.
- Monitor the client's blood pressure when initiating hydralazine/isosorbide dinitrate, and do not administer the medication if systolic blood pressure is less than 90 mm Hg.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking hydralazine/isosorbide dinitrate should:

- Monitor for signs and symptoms of low blood pressure such as dizziness or lightheadedness.
- Get up slowly during the first couple of days of taking the medication in case of orthostatic hypotension.

The client taking hydralazine/isosorbide dinitrate *should not:*

- Take erectile dysfunction medications with this medication because they also contain a nitrate.

Cardiac Glycosides

Cardiac glycosides used to be a first-line therapy in heart failure. Over the years, medications that are safer and more efficacious have been introduced on the market. However, cardiac glycosides may be used as adjunct therapy if first-line medications for heart failure have been optimized and the client still has a reduced ejection fraction and/or symptoms.

Digoxin is the only cardiac glycoside used in heart failure. It affects the sodium-potassium ATPase pump in such a way that causes more calcium to enter the cardiac myocyte. If there is more calcium, then the force of contraction is stronger. Because of this, digoxin is referred to as a *positive inotrope*. Digoxin also stimulates the parasympathetic nervous system, which affects the electrical conduction system of the heart. Parasympathetic stimulation causes the heart to beat less often. This means that there is a longer time for ventricular filling (longer diastole). This helps the heart since the cardiac myocytes receive oxygenated blood during diastole.

Digoxin can have complicated dosage instructions. There often is a loading dose and then a maintenance dose, and factors such as body weight, age, renal function, and concomitant drugs are part of the dosing consideration.

Adverse Effects and Contraindications

Adverse effects include fatal cardiac arrhythmias, sinus bradycardia, sinoatrial block, visual disturbances (yellow or green halo around lights), atrial tachycardia, and rash.

Digoxin has a narrow therapeutic index and a high potential for toxicity. Signs and symptoms of digoxin toxicity include anorexia, nausea, vomiting, visual changes, and cardiac arrhythmias.

Contraindications include acute myocardial infarction, ventricular fibrillation, Wolff-Parkinson-White syndrome, myocarditis, hypokalemia, and hypomagnesemia.

Table 19.18 is a drug prototype table for cardiac glycosides featuring maintenance dosing for digoxin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Cardiac glycoside **Mechanism of Action** Blocks the sodium-potassium ATPase pump, which ultimately causes potassium to remain in the cardiac myocyte longer, leading to a stronger force of contraction Increases parasympathetic stimulation of the heart (mechanism unclear), which decreases heart rate	**Drug Dosage** *Heart failure maintenance dosing:* 0.125–0.5 mg orally once daily.
Indications Continued heart failure symptoms even though first-line medications for heart failure have been optimized **Therapeutic Effects** Increases force of contraction Lowers heart rate	**Drug Interactions** Quinidine Calcium channel blockers Nonsteroidal anti-inflammatory drugs Amiodarone Beta blockers Diuretics (may affect potassium levels, which may potentiate the effectiveness of digoxin) **Food Interactions** Foods high in potassium
Adverse Effects Fatal cardiac arrhythmias Sinus bradycardia Sinoatrial block Visual disturbances (yellow or green halo around lights) Atrial tachycardia Rash	**Contraindications** Acute myocardial infarction Wolff–Parkinson–White syndrome Ventricular fibrillation Hypokalemia Hypomagnesemia

TABLE 19.18 **Drug Prototype Table: Digoxin** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Cardiac Glycosides

Cardiac glycosides can cause fetal death in the second trimester. Clients of childbearing age should not become pregnant while taking cardiac glycosides.

Digoxin has a high potential for toxicity with life-threatening consequences.

Nursing Implications

The nurse should do the following for clients who are taking digoxin:

- Assess pulse for 1 minute prior to administering digoxin. If heart rate is less than 60 beats per minute, do not administer the dose.
- Monitor serum digoxin levels and for signs and symptoms of digoxin toxicity. Also monitor serum potassium levels.
- Assess and monitor for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking digoxin should:

- Monitor their pulse prior to taking digoxin and contact their health care provider if their pulse is <60 beats per minute.
- Monitor for signs of digoxin toxicity (anorexia, nausea, vomiting, green/yellow halos around lights). They should contact their health care provider immediately if they experience these symptoms.
- Notify their health care provider about symptoms such as dizziness, lightheadedness, or fainting because these could be related to low blood pressure.

Ivabradine

Ivabradine (Corlanor) was introduced fairly recently as an adjunct therapy for clients who are optimized on first-line heart failure medications but still have a reduced ejection fraction and/or symptoms.

Ivabradine is an **I_f current inhibitor** that affects the cardiac pacemaker current (I_f) directly, causing a decreased heart rate and longer diastole. A decreased heart rate lowers the heart's demand for oxygen, and longer diastole allows for increased oxygenation of cardiac myocytes.

Adverse Effects and Contraindications

Adverse effects include bradycardia, atrial fibrillation, elevated blood pressure, heart block, prolonged QT segment, torsade de pointes, and luminous phenomena (enhanced brightness of light or halo around light). Fetal toxicity has occurred in animal studies.

Contraindications include acute decompensated heart failure, hypotension, history of conduction problems (such as sick sinus syndrome), bradycardia, and liver dysfunction. Ivabradine has been shown to cause fetal toxicity in animal studies; therefore, clients should not be pregnant or become pregnant while taking ivabradine.

Table 19.19 is a drug prototype table featuring ivabradine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class I_f current inhibitor **Mechanism of Action** Blocks the hyperpolarization-activated cyclic nucleotide-gated (HCN) channel that regulates cardiac pacemaker current	**Drug Dosage** *Heart failure:* 5–7.5 mg orally twice daily; maximum dose: 7.5 mg orally twice daily.
Indications Stable heart failure with an ejection fraction ≤35% to reduce the risk of hospital admission for worsening heart failure **Therapeutic Effects** Slows heart rate Allows for longer period of diastole Increases oxygenation of cardiac myocytes	**Drug Interactions** Metabolized by CYP450 enzymes/verapamil Diltiazem **Food Interactions** Grapefruit juice
Adverse Effects Bradycardia Atrial fibrillation Elevated blood pressure Heart block Prolonged QT segment Torsade de pointes Luminous phenomena (enhanced brightness of light or halo around light) Fetal toxicity	**Contraindications** Acute decompensated heart failure Hypotension History of conduction problems (e.g., sick sinus syndrome, etc.) Bradycardia Liver dysfunction Pregnancy

TABLE 19.19 **Drug Prototype Table: Ivabradine** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Ivabradine

Clients of childbearing age should take measures not to become pregnant while taking ivabradine due to teratogenic effects (causing harm to embryo or fetus).

Nursing Implications

The nurse should do the following for clients who are taking ivabradine:

- Tell clients to report dizziness or shortness of breath because those may be related to bradycardia and/or atrial fibrillation.
- Inform clients that ivabradine must be taken with food.
- Teach clients about food and drug interactions.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking ivabradine should:

- Report feeling dizzy, lightheaded, or an erratic heartbeat to the health care provider.
- Avoid grapefruit juice.
- Notify the health care provider if pregnant, planning on getting pregnant, or breastfeeding prior to starting ivabradine.

Chapter Summary

This chapter focused on heart failure drugs. Heart failure was defined and described per the AHA/ACC/HFSA 2022 Guidelines. Heart failure is a decrease in cardiac output. Heart rate and stroke volume are two components of cardiac output. Stroke volume is composed of preload, afterload, and contractility. The renin-angiotensin-aldosterone system was described, and how the system impacts cardiac output was explained.

Common heart failure drug classifications were covered in the chapter. Drug classifications covered included angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), angiotensin receptor/neprilysin inhibitors (ARNIs), mineralocorticoid receptor inhibitors (MRAs), beta-adrenergic blockers, sodium-glucose cotransport inhibitors (SGLT2Is), and diuretics. Adjunct drug classifications covered in this chapter included hydralazine/isosorbide dinitrate, cardiac glycosides, and ivabradine.

Key Terms

afterload the amount of force the left ventricle must push against

angiotensin I a protein in blood that promotes aldosterone secretion and raises blood pressure

angiotensin II a protein in the blood that causes the muscular walls of the arterioles to constrict and narrow, thereby increasing blood pressure

angiotensin II receptor blocker (ARB) a classification of drugs that bind to and inhibit angiotensin II type I receptors

angiotensin receptor/neprilysin inhibitor (ARNI) a classification of drugs that bind to and inhibit angiotensin II type I receptors and inhibit the breakdown of BNP

angiotensin-converting enzyme (ACE) inhibitor a classification of drugs that block the body's production of angiotensin II; causes vasoconstriction and inhibits the reuptake of norepinephrine, which stimulates catecholamine release

beta-adrenergic blocker a classification of drugs that inhibit chronotropic, inotropic, and vasoconstrictor response to catecholamine, epinephrine, and norepinephrine by exerting effects on adrenergic receptors beta 1, beta 2, and alpha

cardiac glycoside a classification of drugs that decrease heart rate and increase cardiac contraction by blocking the sodium-potassium ATPase pump

cardiac output the product of the heart rate and stroke volume, or the amount of blood ejected with each heartbeat in a given period of time

contractility the ability of the ventricle to squeeze or pump blood

diuretic a classification of drugs that induce sodium loss and increase urine flow; typically used to treat hypertension, heart failure, and volume overload states

ejection fraction the fraction of blood that is pumped out of the heart with each beat

heart failure a clinical syndrome that occurs when the heart does not generate adequate cardiac output

heart failure with preserved ejection fraction (HFpEF) occurs when the fraction of blood ejected by the left ventricle has not changed but cardiac output is inadequate; often due to stiffness of the ventricular muscle

heart failure with reduced ejection fraction (HFrEF) occurs when the fraction of blood ejected by the left ventricle is actually reduced; often due to damage to the left ventricular muscle through long-standing hypertension or coronary artery disease

heart rate the number of times each minute the heart beats

I_f current inhibitor a classification of drugs that inhibit cardiac pacemaker current (I_f), which causes lowered heart rate

ivabradine medication used in heart failure that regulates heart rate and causes increased diastolic filling time, which results in increased cardiac output

mineralocorticoid receptor antagonist (MRA) a classification of drugs that cause diuresis and other effects by binding to receptors in the nephron so that aldosterone is not able to affect it and cause sodium and water reabsorption

preload the volume of blood returning to the heart

renin-angiotensin-aldosterone system (RAAS) a compensatory mechanism the body activates during hypotension (when the blood pressure is low)

sodium-glucose cotransport inhibitor (SGLT2I) a classification of drugs that cause diuresis and other benefits that block the reabsorption of sodium and glucose in the proximal tubule of the nephron

stroke volume the volume of blood pumped out of the left ventricle of the heart during each systolic cardiac contraction

Review Questions

1. What are the components of cardiac output?
    a. Blood pressure and systemic vascular resistance
    b. Heart rate and systemic vascular resistance
    c. Circulatory function and respiratory rate
    d. Heart rate and stroke volume

2. A client is being prescribed lisinopril at discharge from the hospital by the health care provider. The discharge instructions by the nurse should include that lisinopril acts by doing which of the following?
    a. Inhibits beta 1 and beta 2
    b. Inhibits angiotensin-converting enzyme
    c. Prevents the release of angiotensin
    d. Blocks angiotensin II from activating angiotensin receptors

3. A client has been prescribed lisinopril 7.5 mg twice daily. The tablets are 2.5 mg. How many tablets should the client take per dose?
    a. 1 tablet
    b. 2 tablets
    c. 3 tablets
    d. 4 tablets

4. A client with heart failure who had been taking valsartan recently had the medication switched to sacubitril/valsartan. The client understands how valsartan works but is confused about sacubitril. The nurse explains that sacubitril:
    a. Lowers heart rate to allow for more oxygen to get to the heart muscle tissue
    b. Inhibits angiotensin-converting enzyme, which lowers blood pressure
    c. Helps BNP stay in the system longer, which lowers blood pressure
    d. Causes nitric oxide to be released in smooth muscles, which lowers blood pressure

5. A client is taking valsartan, carvedilol, and spironolactone daily. What monitoring should the nurse educate the client about to ensure safe medication administration?
    a. Electrolytes, because two of the medications cause an elevation in potassium
    b. Electrolytes, because two of the medications cause a decrease in potassium
    c. Glucose, because the combination of medications can lower blood glucose
    d. Uric acid, because the combination of medications can increase uric acid

6. A client with heart failure had a new medication added to their regimen, dapagliflozin. The nurse recognizes that this medication is effective through which mechanism?
    a. Inhibiting alpha receptors in the arteries
    b. Enhancing the release of BNP
    c. Inhibiting sodium and glucose reabsorption
    d. Enhancing beta-1 receptors in the heart

7. A client with heart failure has been prescribed furosemide 60 mg every morning. The tablets come in 40 mg. How many tablets should the client take each morning?
    a. ½ tablet
    b. 1 tablet
    c. 1½ tablets
    d. 2 tablets

8. A Black client with heart failure has recently had their medication regimen changed to the combination medication hydralazine and isosorbide dinitrate. What education does the nurse provide the client?

a. This medication regimen will increase afterload.
b. These two medications increase systemic vascular resistance.
c. Hydralazine/isosorbide dinitrate works better than other heart failure medications for Black clients.
d. This medication combination will cause better diuresis.

9. The nurse is caring for a client with heart failure who takes digoxin. Which assessment finding should the nurse report to the health care provider prior to administering the drug?
a. Blood pressure 124/78 mm Hg
b. Respiratory rate 16 breaths/minute
c. Temperature 98.2°F
d. Heart rate 54 beats/minute

10. A nurse is providing education to a client who has a new prescription for ivabradine. The nurse knows the client has understood the instructions when the client makes which statement?
a. "I will stop eating green, leafy vegetables."
b. "I will stop drinking grapefruit juice."
c. "I will take my blood pressure right before I take this medication."
d. "I will take this medication right before I go to bed."

CHAPTER 20

Anticoagulant, Antiplatelet, and Thrombolytic Drugs

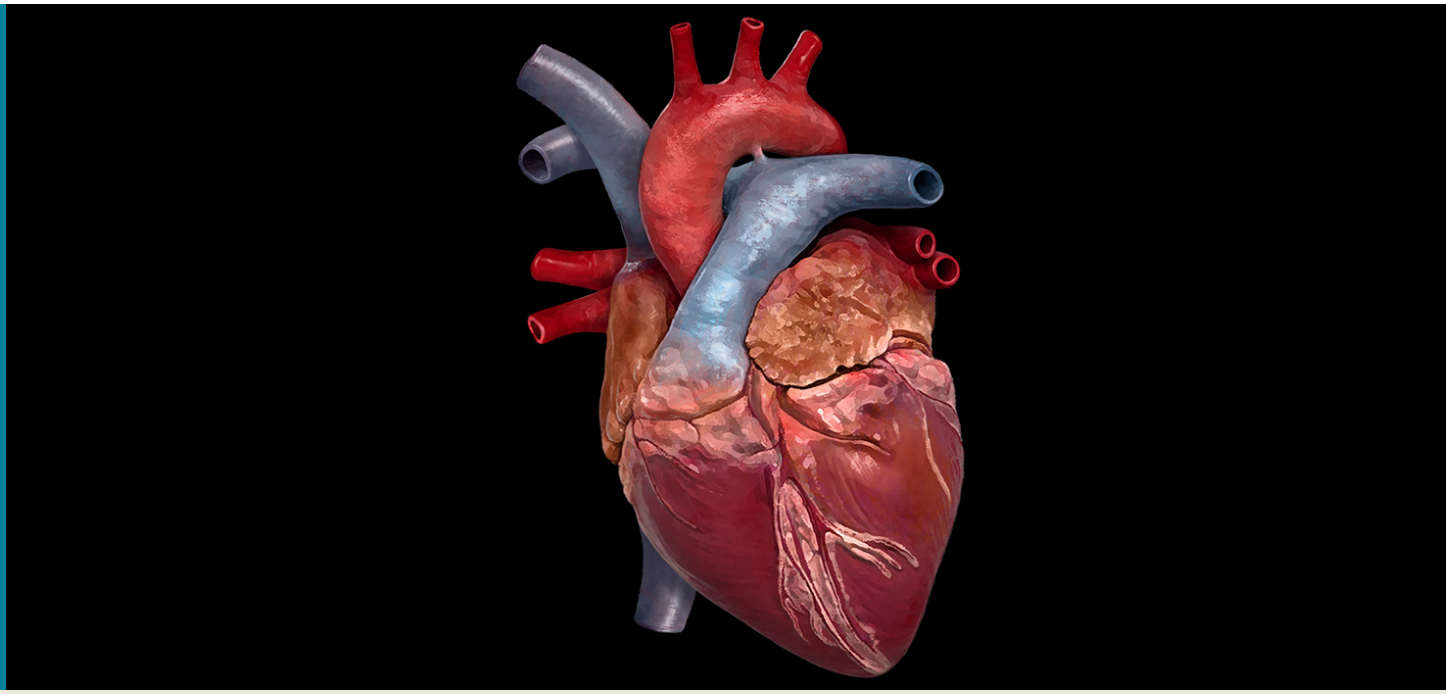


FIGURE 20.1 The heart is the primary organ of the cardiovascular system, controlling circulation and blood flow for the entire body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Blood moves through the cardiovascular system to deliver oxygen and nutrients to the various tissues, including those that make up the body's organs. It is pumped by the heart into arteries, which carry oxygenated and nutrient-rich blood to each tissue. Arteries branch into smaller arteries called arterioles, then into capillaries. Capillaries are thinned-walled blood vessels that facilitate gas exchange, or the exchange of oxygen for carbon dioxide in the tissues. Blood is collected into small veins called venules, which drain into larger veins that eventually bring blood back to the heart for oxygenation. See Heart Failure Drugs for more information on the circulatory system.

Blood is made up of many components, such as **erythrocytes** (red blood cells), leukocytes (white blood cells, which are important in the immune system), and **platelets**. Erythrocytes contain **hemoglobin**, which is the substance that binds with oxygen and facilitates its transport in the blood. Platelets are the sticky substances in the blood that form a scab when a client has a cut or injury. More information on platelets will be discussed later in this chapter. Blood also contains plasma, which is the fluid surrounding the cellular components of blood and is made up of water, electrolytes, and proteins.

The amount of the various components of blood can be monitored by a laboratory blood test called a **complete blood count (CBC)**. The CBC measures the amount of red blood cells, white blood cells, hemoglobin, **hematocrit**,

and platelets. Hematocrit is another way to assess the amount of red blood cells by measuring the ratio of red blood cells to the overall volume of blood. Low hemoglobin and/or hematocrit can signal blood loss or anemia, among other etiologies.

20.1 Introduction to Clotting and Coagulation

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 20.1.1 Explain the pathophysiology of thrombus formation.
- 20.1.2 Identify the clinical manifestations of thrombus formation.
- 20.1.3 Identify the etiology and diagnostic studies related to thrombus formation.

The ability of the blood to form clots in response to tissue damage is essential for **hemostasis**, or the body's ability to stop bleeding. However, clot formation also underpins many **thrombosis**-related diseases such as acute myocardial infarction, stroke, and deep vein thrombosis. A client with naturally occurring decreased clotting times is described as **hypercoagulable**.

Blood Coagulation

Human blood moves as a fluid; however, when injury occurs, hemostasis is accomplished in two major ways: primary hemostasis and secondary hemostasis. Primary hemostasis is the process of platelet adhesion to form a platelet plug, or platelets that are aggregated on the injured vessel wall or tissues. Platelets can be activated in response to collagen released during tissue damage or by a number of other substances. A few of the substances most important for pharmacology are highlighted below and are shown in Figure 20.2:

- Thromboxane A2, synthesized by the cyclooxygenase pathway
- Adenosine diphosphate, which interacts with P2Y12 receptors on the platelet surface
- Thrombin, produced in the coagulation cascade described below
- Von Willebrand factor and fibrinogen, which bind to the glycoprotein IIb/IIIa (GPIIbIIIa) receptor to facilitate platelet adhesion to other platelets and to the blood vessel wall

Each of these activation steps represents a potential drug target in treatment of pathologic thromboses; they will be expanded upon within the text for the relevant drugs.

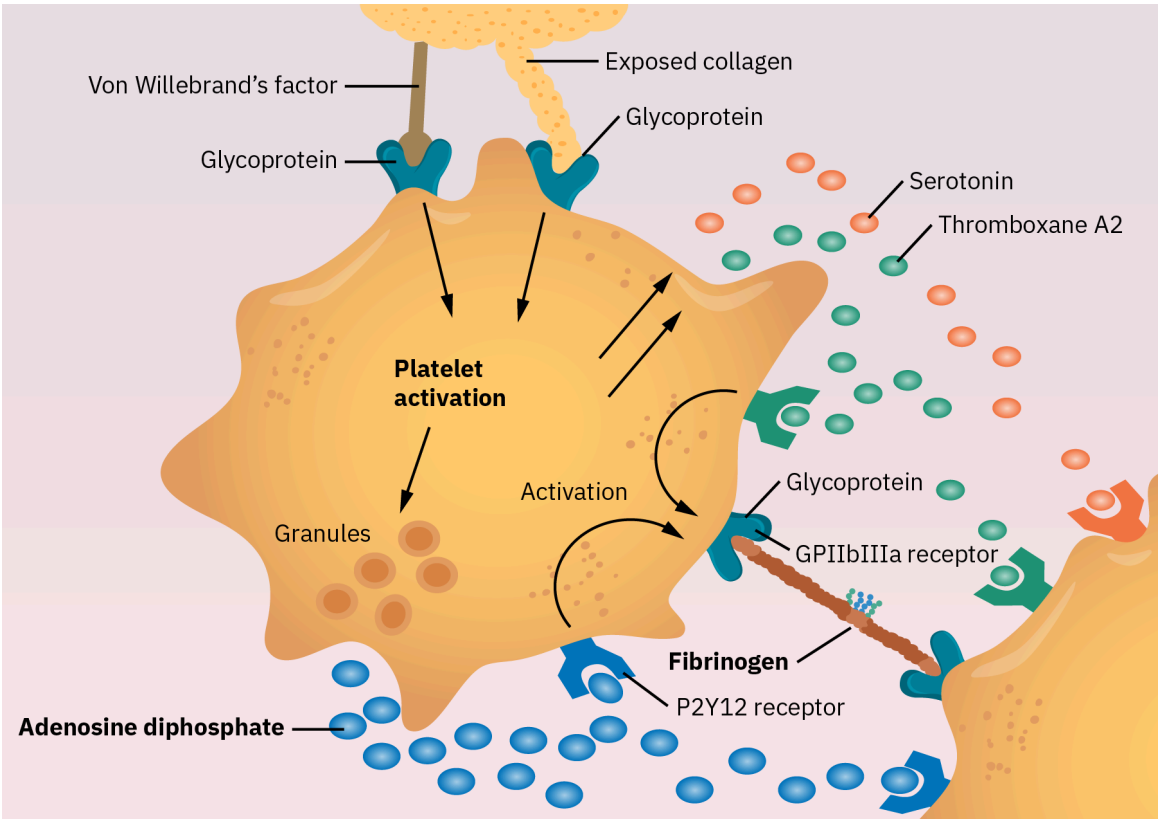


FIGURE 20.2 Platelet activation occurs through thromboxane A2, adenosine diphosphate, thrombin, von Willebrand's factor, and fibrinogen, among other substances. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Upon tissue injury, secondary hemostasis can be activated via the **coagulation cascade**. The coagulation cascade can be thought of as a chain reaction. The coagulation cascade is made up of **clotting factors**, which are proteins that work to activate different parts of the coagulation cascade. The factors are named numerically with Roman numerals (e.g., factor X, factor VII). An activated form of a factor is denoted by "a" suffix (e.g., factor Xa, factor VIIa). Figure 20.3 depicts the clotting cascade; it may be helpful to follow the figure simultaneously while reading through the text.

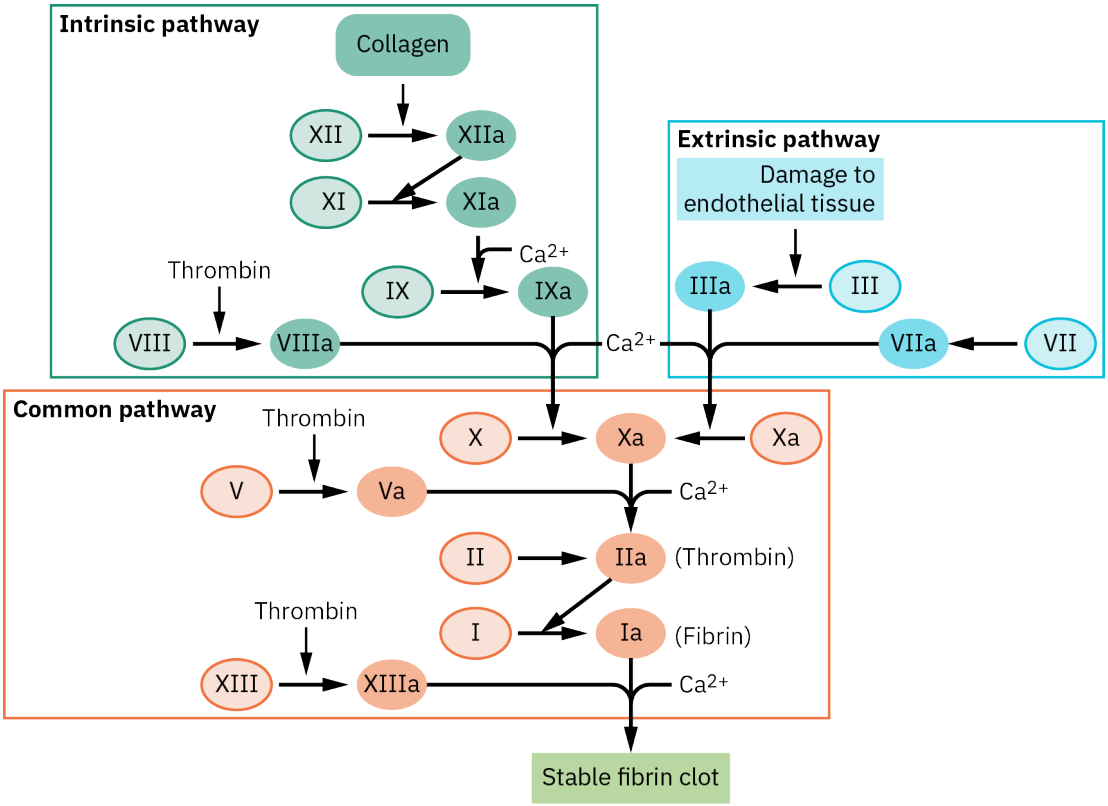


FIGURE 20.3 The coagulation cascade can be activated by either the intrinsic or extrinsic pathways. Clotting factors form a chain reaction and converge on a common pathway that ends in formation of a stable fibrin clot. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The coagulation cascade can be activated by either the intrinsic pathway or extrinsic pathway, which converge on a common final pathway. Although they are discussed as separate pathways, the physiology is less linear and more complex, with significant crossover and both pathways being activated in response to tissue damage.

- The extrinsic pathway is activated by injury to blood vessels, which release tissue factor when damaged. Tissue factor works with factor VIIa to activate factor X to factor Xa, which is part of the common pathway.
- The intrinsic pathway is activated by collagen that is exposed when there is endothelial damage. Collagen facilitates the activation of factor XII. Factor XIIa then facilitates the activation of factor XI, which in its activated form facilitates the activation of factor IX. Factor IXa and factor VIIIa work together to facilitate activation of factor X.
- The common pathway begins with factor X. Recall from above that factor X is activated by both the intrinsic and extrinsic pathways. Factor Xa facilitates the activation of factor II, which is also known as thrombin. Thrombin facilitates the activation of fibrinogen to fibrin. Thrombin also has other roles within the clotting cascade; it activates factor VIII in the intrinsic pathway and factor V in the common pathway. Thus, activation of thrombin contributes to increased upstream activation as well, which continues down the cascade and activates more thrombin. Fibrin monomers link together to form fibers and branches that make up a solid fibrin clot.

It is noteworthy that many other substances are involved in synthesis and regulation of the clotting cascade. Vitamin K, a vitamin present in foods such as green, leafy vegetables, is a cofactor needed for synthesis of clotting factors II, VII, IX, and X. Calcium is also necessary for activation of several clotting factors.

Coagulation is in homeostatic balance with **fibrinolysis**, or breakdown of fibrin, as shown in Figure 20.4. This is accomplished when the enzyme tissue plasminogen activator (tPA) facilitates conversion of plasminogen to plasmin, which degrades fibrin. Other natural anticoagulants include proteins C and S, which work together to inhibit the activation of many clotting factors including factors VIIIa, Va, X, and prothrombin; antithrombin, which inhibits the action of many clotting factors including factor Xa and thrombin; and tissue factor pathway inhibitor (TFPI), which inhibits the action of factor Xa.

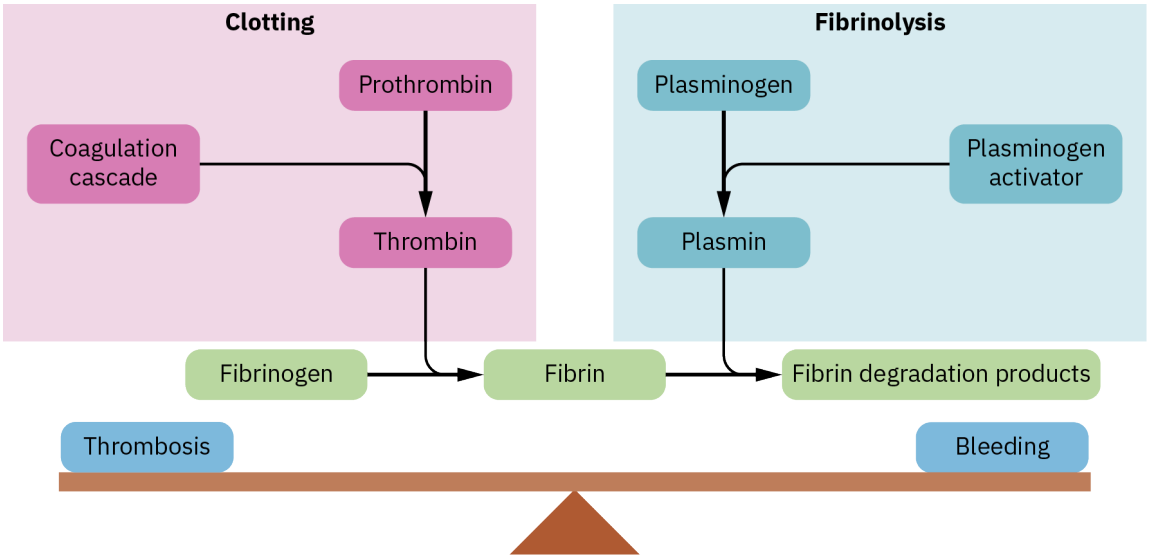


FIGURE 20.4 Clotting and fibrinolysis are in constant balance. Excessive activation of the coagulation cascade can lead to thrombosis, the formation of a clot inside a blood vessel that can block blood flow. Excessive fibrinolysis, mediated by plasmin, can lead to bleeding. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

SPECIAL CONSIDERATIONS

Factor V Leiden

Factor V Leiden is a blood-clotting disorder that increases the client's risk of thrombosis. It results from a genetic mutation that causes a change in factor V, making it less susceptible to inactivation. Clients with Factor V Leiden cannot change their genetics, but they can work to minimize their other risk factors for thrombosis by maintaining a healthy weight, exercising regularly, and avoiding smoking. These clients should also be vigilant about moving and taking breaks during travel. If these clients experience a clot, they will likely need anticoagulant therapy for the remainder of their life. The National Blood Clot Alliance website (https://openstax.org/r/stoptheclot) provides more information.

Thrombus Formation

The pathologic formation of thrombi (plural of thrombus) occurs as the result of endothelial injury, hypercoagulability, and stasis of blood flow; this is known as Virchow's Triad and is depicted in Figure 20.5. Endothelial injury activates clotting as described above and occurs due to events such as catheter placement, surgery, or trauma (Ashorobi, 2022). Hypercoagulability refers to a prothrombotic state due to circumstances such as an excess of clotting factors or relative insufficiency of natural anticoagulants. Abnormal blood flow can occur due to prolonged immobility (such as during travel, surgeries, or hospitalization), atherosclerosis within a blood vessel, or an abnormal heart rhythm called atrial fibrillation, where blood pools in the atria because there is no organized contraction of the chambers.

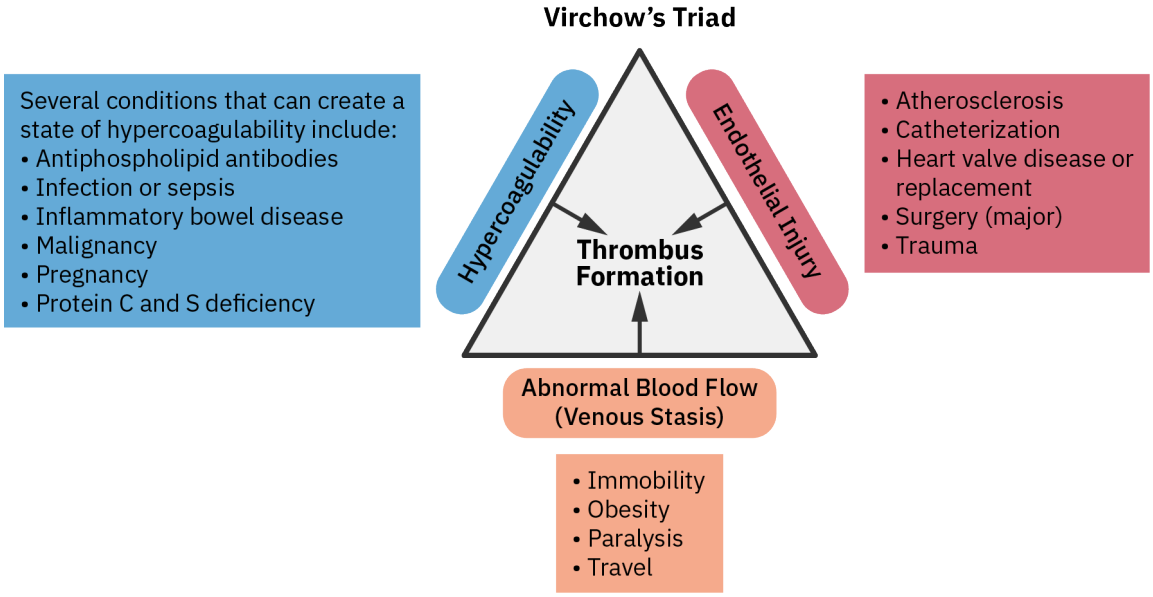


FIGURE 20.5 Virchow's Triad describes the causes of clot formation. (See Kushner, et al., 2022, and McLendon, et al., 2023; attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

While formation of a clot can be lifesaving during bleeding events, formation of a thrombus can occlude a blood vessel, prohibiting the delivery of blood to downstream tissues. The most common types of thrombi are described below, although this list is not all-inclusive.

Deep Vein Thrombosis and Pulmonary Embolism

A **deep vein thrombosis (DVT)** is a blood clot that forms within a vein. It most commonly occurs within the legs but can occur elsewhere, such as the pelvis and arms. The clot can break off, travel through the circulatory system, and lodge within the lungs, causing a **pulmonary embolism (PE)**, which can be life-threatening. Risk factors for DVTs include stasis of blood flow caused by confinement to a bed, limited movement, sitting for a long time (such as during travel), or paralysis; increased estrogen caused by oral contraception or pregnancy; certain medical conditions such as cancer; personal or family history of DVT; increased age; obesity; catheter placement; or genetic clotting disorders. Clients with a DVT may experience swelling, pain, redness, and tenderness at the site of the clot (usually in the leg). Clients with a PE often describe chest or back pain and have difficulty breathing, tachycardia, hemoptysis (coughing up blood), and if severe, hemodynamic instability (Centers for Disease Control and Prevention [CDC], 2020). Clients who experience a deep vein thrombosis typically need to be treated with anticoagulant medications. A pulmonary embolism is commonly diagnosed with a computed tomography pulmonary angiogram (CTPA), a specialized type of x-ray that allows visualization of the pulmonary vessels. A ventilation/perfusion scan (also known as a VQ scan) is another type of imaging test that can help diagnose a pulmonary embolism by assessing air flow (ventilation) and blood flow (perfusion) in the lungs.

Ischemic Stroke (Cerebral Infarction)

When a clot obstructs blood flow to the brain, it can cause an **ischemic stroke**. Two types of ischemic stroke are atherosclerotic and embolic. An atherosclerotic ischemic stroke can be caused by a buildup of fatty substances, cholesterol, and other substances that can narrow the artery and cause blood clots to form. Risk factors for atherosclerotic stroke include male sex, family history of premature cardiovascular disease, hypercholesterolemia, cigarette smoking, hypertension, diabetes mellitus, obesity, and physical inactivity. Clients who experience an atherosclerotic ischemic stroke may also need antiplatelet therapy in addition to treatment of any contributing disease states.

An embolic ischemic stroke (also known as a *cerebral embolism*) occurs from a blood clot that forms elsewhere in the body. It can be caused by a dysrhythmia called atrial fibrillation (American Stroke Association, 2021) or by clots that form on prosthetic heart valves. In atrial fibrillation, abnormal blood flow within the left side of the heart can lead to clot formation, which can travel out the aorta and lodge within the blood vessels of the brain, occluding blood flow. In clients with atrial fibrillation, the CHA_2D_2-VASc score (Parsons et al., 2017) can help estimate stroke risk. The scale includes a point system for the following variables: age, sex, heart failure, hypertension, personal

history of thromboembolism, vascular disease, and diabetes. It can be calculated by hand or by using an online stroke risk calculator (https://openstax.org/r/mdcalc). Clients who have atrial fibrillation or certain prosthetic heart valves usually are treated with an anticoagulant to decrease the risk of embolic stroke. A computed tomography (CT) scan of the brain with contrast allows visualization and diagnosis of both types of stroke.

Myocardial Infarction and Coronary Artery Disease

Clients with atherosclerosis in their coronary arteries are said to have coronary artery disease. The disease states of coronary artery disease and myocardial infarction are expanded upon in the chapters Antihypertensive and Antianginal Drugs and Cardiac Emergency and Shock Drugs. Clients with acute myocardial infarction and coronary artery disease usually are treated with antiplatelet medications. This is especially true after a coronary artery stent is placed. A coronary artery stent is a wire caging that props open a narrowed coronary artery. These require treatment with two concomitant antiplatelet medications for a period of time after stent placement to prevent clots from forming on the stent. While there are many ways to detect a myocardial infarction or coronary artery disease, clots can be directly visualized using coronary angiography during a left-heart catheterization.

20.2 Anticoagulants

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 20.2.1 Identify the characteristics of the anticoagulant drugs used to treat thrombus formation.
- 20.2.2 Explain the indications, actions, adverse reactions, and interactions of the anticoagulant drugs used to treat thrombus formation.
- 20.2.3 Describe nursing implications of anticoagulant drugs used to treat thrombus formation.
- 20.2.4 Explain the client education related to anticoagulant drugs used to treat thrombus formation.

Anticoagulants Used as Blood Thinners

Anticoagulants are commonly referred to as *blood thinners*. They work in different parts of the coagulation cascade to decrease the propensity of the blood to form a clot. There are many types of anticoagulants that work in various ways and can be administered by intravenous, subcutaneous, or oral routes, depending on clients' circumstances and needs. One important note is that anticoagulants do not dissolve existing clots. Instead, they prevent further clot formation and allow the body to naturally dissolve any existing clots over time. **Thrombolytics**, or drugs that dissolve existing clots, will be discussed later in this chapter.

Many anticoagulants have a narrow therapeutic index, meaning that the dose must be individualized, monitored, and controlled to ensure that clients do not experience therapeutic failure (e.g., a clotting complication from their disease) or adverse events. Because of this, anticoagulants are classified as high-alert medications (Institute for Safe Medication Practices, 2018). High-alert medications often have specific nursing precautions during use. Many hospitals require manual independent double-checks and utilize automated alerts to ensure safe use. Additionally, extra monitoring is often required to ensure the drug levels are appropriate and the blood is not "too thin" (over-anticoagulated) or "too thick" (under-anticoagulated). The specific anticoagulant used and the clinical scenario determine which drug-specific monitoring may be required. Some of the monitoring parameters are:

- **Partial thromboplastin time (PTT) or activated partial thromboplastin time (aPTT)**: A PTT is a laboratory test obtained via venous blood sample that measures how much time the blood takes to clot. A PTT of a non-anticoagulated client without a clotting disease is 25–35 seconds (Rountree & Lopez, 2018). A higher PTT indicates that the blood is thinner, less likely to form a clot, and the client is more prone to bleeding. An aPTT is considered a more sensitive version of a PTT.
- **International normalized ratio (INR)**: This is a laboratory test obtained via venous blood sample that provides another measurement of the time it takes for the blood to clot, calculated using the **prothrombin time (PT)**. The INR of an un-anticoagulated client without a clotting disease is 1. It should be noted that point-of-care machines are available for INR monitoring so that clients can obtain results in real time, either in a clinic or at home. A higher INR indicates that the blood is thinner and less likely to form a clot, and the client is more prone to bleeding.
- **Anti-factor Xa level (Anti-Xa)**: The anti-Xa level provides a measurement of the concentration of drugs that inhibit factor Xa in the clotting cascade. A higher anti-Xa level indicates that there is more drug in the blood,

the blood is thinner and less likely to form a clot, and the client is more prone to bleeding.

- **Activated clotting time (ACT)**: The ACT is another way to measure clotting time. This test is frequently done as a point-of-care test and can be done during procedures or surgeries where immediate knowledge of anticoagulant effect is necessary. This is often used in the cardiac catheterization laboratory and during cardiopulmonary bypass in open-heart surgery. A higher ACT indicates that the blood is thinner and less likely to form a clot, and the client is more prone to bleeding.

There are many different anticoagulants, available as injectable or oral medications.

Injectable Anticoagulants

Injectable anticoagulant medications have the advantage of avoiding the oral route of administration, which may be important for clients who are unable to take oral medications or have issues with gastrointestinal absorption. The most common injectable anticoagulants are heparin and the low molecular weight heparin, enoxaparin.

Heparin

Heparin is an injectable anticoagulant used primarily in the hospital setting. It is FDA approved for the treatment and prevention of thromboembolism. Heparin works by inactivating clotting factors in the coagulation cascade. It binds to antithrombin and the complex inactivates IIa (thrombin), Xa, IXa, XIa, and XIIa. Heparin is primarily administered via an intravenous or subcutaneous route. Subcutaneous use is limited because the absorption by that route is erratic and the bioavailability, or amount of drug that makes it into systemic circulation, is low. The dosing for heparin is complicated. For treatment of a thromboembolism, it is typically given as a weight-based continuous infusion that is titrated based on client response. Response is measured using either the PTT or anti-Xa level, depending on the institutional protocol.

The goal level of heparin varies based on the institution, indication, and client-specific doses. The goal level typically corresponds to 1.5–2.5 times the baseline PTT. Typically, monitoring of the anti-Xa level or PTT level is completed every 6 hours during an infusion. If the PTT or anti-Xa level is lower than the goal, it is described as subtherapeutic, meaning the blood is "too thick." In this situation, a bolus dose may be given and/or the infusion rate increased with subsequent monitoring. If the PTT or anti-Xa level is higher than the goal, it is described as supratherapeutic, meaning the blood is "too thin." The infusion may be held for a period of time and/or the infusion rate decreased. Some institutions have protocols for nurse-driven management of heparin. In these protocols, the nurse monitors the PTT or anti-Xa level as directed in the protocol, then adjusts the dose as directed without a new order from the provider.

An example of a heparin dosing protocol is shown in Table 20.1, utilizing PTT monitoring and potential dose adjustment every 6 hours.

PTT	Dosing
	Initial dose: 80 units/kg bolus, then 18 units/kg/hr.
PTT <35 seconds	80 units/kg bolus, then increase rate by 4 units/kg/hr.
PTT 35–45 seconds	40 units/kg bolus, then increase rate by 2 units/kg/hr.
PTT 46–70 seconds	No change.
PTT 71–90 seconds	Decrease infusion rate by 2 units/kg/hr.
PTT >90 seconds	Interrupt infusion for 1 hour, then decrease infusion rate by 3 units/kg/hr.

TABLE 20.1 A Sample Heparin Dosing Protocol (source: Hirsh et al., 2001)

Heparin can also be monitored using the ACT, although less frequently. This is typically limited to monitoring during procedures and surgeries by a point-of-care device. It allows for quick fine-tuning of the heparin dosage in real time.

If long-term anticoagulation is needed, an oral anticoagulant is usually started. The transition to oral anticoagulation depends on the agent being initiated. For example, warfarin takes several days to achieve therapeutic anticoagulation, so overlap with a parenteral agent (e.g., continuation of heparin or initiation of enoxaparin) is warranted until then. Other chronic agents may take action immediately; thus, heparin can be discontinued without overlap.

Heparin-induced thrombocytopenia (HIT) is a rare although major complication of heparin therapy. It is

characterized by an immune-mediated decrease in platelets, often with concomitant thrombosis. Although the platelets are decreased, the client is in a highly hypercoagulable state. Heparin must be discontinued immediately, and alternative anticoagulation with a non-heparin-based anticoagulant is required. Argatroban, an intravenous direct thrombin inhibitor anticoagulant, is FDA approved to treat HIT. Bivalirudin is another intravenous direct thrombin inhibitor anticoagulant that has been studied for off-label use in treating clients with HIT. After the acute phase of HIT, clients can be transitioned to a long-term oral or subcutaneous non-heparin anticoagulant. Clients with a history of HIT should not receive heparin in the future. Other adverse effects of heparin include hyperkalemia and osteoporosis with prolonged use.

CLINICAL TIP

Assess for Heparin-Induced Thrombocytopenia (HIT)

It can be difficult to predict which clients are experiencing HIT. The 4T scoring system estimates the risk for HIT based on the degree, timing, and potential etiology of the client's platelet decrease, and the presence of thrombosis. Online calculators for the 4T score (https://openstax.org/r/mdcal) are available. The diagnosis of HIT is more likely and should be considered when the platelet count drops by 50% or more.

SAFETY ALERT

Heparin Concentrations

There are many different heparin products and strengths available, which can lead to medication errors (https://openstax.org/r/ismp) if the incorrect concentration or formulation is selected.

Enoxaparin

Enoxaparin is a derivative of heparin and is referred to as a low molecular weight heparin. It is FDA approved to treat thromboembolism and acute coronary syndromes. It is also approved to decrease the rate of thromboembolism after surgery and during prolonged immobilization. It works similarly to heparin; however, it targets factor Xa specifically. Enoxaparin can be administered intravenously and subcutaneously. A major advantage to using enoxaparin as compared to heparin is that it has more reliable subcutaneous absorption and a longer half-life; thus, it can more reliably be administered as an intermittent subcutaneous injection without continuous titration. It can be self-administrated by the client at home using a pre-filled syringe. Under most circumstances, specific monitoring is not required. A major disadvantage of enoxaparin is that it is eliminated by the kidneys and therefore the dose must be adjusted or the drug must be avoided in those with kidney dysfunction. Although enoxaparin can cause HIT, the incidence is less than therapy with heparin.

As enoxaparin can be self-administered by the client, there are many client education points to emphasize with its use. The client should:

- Learn appropriate injection technique. The manufacturer for Lovenox provides a client-education video (https://openstax.org/r/lovenox) for injection. The product labeling also includes pictorial representations of injection technique.
- Inject into subcutaneous abdomen and alternate injection sites between the left and right anterolateral and left and right posterolateral abdominal wall.
- Inject into a skin fold held between the thumb and forefinger, holding the skin fold throughout the injection.
- Avoid injecting through clothing or into skin that is bruised or scarred.
- Avoid ejecting the air bubble from the syringe.
- Avoid rubbing the injection site after administration.

Oral Anticoagulants

As their name indicates, oral anticoagulants are administered by the oral route. They have the benefit of convenience for home administration and can be helpful for clients with a fear of needles. Warfarin was the first oral anticoagulant medication, approved in 1954. Newer oral anticoagulant medications, referred to as direct-acting oral anticoagulants (DOACs), came on the market in 2010 and have supplanted much of warfarin use. These newer

medications include dabigatran, apixaban, rivaroxaban, and edoxaban.

Warfarin

Warfarin is an oral anticoagulant that is FDA approved to treat and prevent thromboembolism disorders. Warfarin inhibits the production of vitamin K in the body. Vitamin K is needed for production of clotting factors II, VII, IX, and X. When warfarin is administered, the production of those clotting factors is decreased, which leads to an anticoagulated state. It is available as an oral tablet in many strengths to allow for individualized dosing. Each tablet of the same dose is the same color regardless of manufacturer. For example, all warfarin 1 mg tablets are pink. (For more information, see this online chart of standard warfarin tablet colors and strengths (https://openstax.org/r/ucsd). Dosing of warfarin is individualized, variable, and complicated by pharmacokinetic properties and food and drug interactions. Doses are titrated based on INR. The therapeutic goal INR varies per indication but is usually 2–3. Some clients with mechanical heart valves have an INR goal of 2.5–3.5. Clients are typically started on anywhere from 1–10 mg of warfarin depending on client-specific factors including genetic polymorphisms, if known. The full effect of warfarin is not apparent until 5–7 days after administration; thus, dose adjustments based on INR are limited before that time frame. Warfarin also has a long half-life, and effects can persist for 5 or more days after discontinuation. Many clients who take warfarin attend clinics that specialize in warfarin dose adjustments. For most clients, the INR is monitored frequently during initiation and during any lifestyle or medication changes.

Warfarin has numerous drug and food interactions. Drugs interacting with warfarin can cause an increase in bleeding risk via effects on the metabolism of warfarin through the cytochrome P450 enzyme or through a decrease in production of vitamin K. Some notable interacting drugs/drug classes are listed in Table 20.3; however, this list is not inclusive and merely points out a few examples. It is important for clients who take warfarin to maintain a consistent amount of vitamin K intake. Since warfarin decreases vitamin K production, dietary intake of vitamin K opposes the anticoagulant effect and can decrease warfarin's effect. Conversely, if a client regularly consumes vitamin K foods but abruptly stops, their blood can quickly become over-anticoagulated.

Because of all the extra monitoring and food and drug interaction, warfarin requires in-depth client education. The nurse should instruct the client to:

- Maintain a consistent amount of vitamin K in their diet. It does not need to be avoided altogether, but a consistent amount is important. Green, leafy vegetables are known for their high vitamin K content. Some of these foods are broccoli, brussels sprouts, coleslaw, kale, and collard greens, and they should not be eaten in excess. The American Heart Association provides a list of foods that are high and low in vitamin K (https://openstax.org/r/heart).
- Be educated on drug interactions that can occur. Any time a new medication is started, all involved providers should be notified so that the warfarin dose and monitoring can be proactively addressed. This is especially important with acute antibiotics that may otherwise go unnoticed when prescribed by a new provider.
- Send for a guide similar to this AHA warfarin guide (https://openstax.org/r/arrhythmia) to help them manage their medication.
- Have their liver enzymes monitored for early signs of hepatotoxicity and jaundice.
- Have their hemoglobin and hematocrit levels checked regularly.
- Abstain from alcohol to reduce risk of bleeding, as alcohol can thin the blood.
- Wear a medical alert bracelet indicating warfarin use.
- Use a soft-bristle toothbrush and an electric razor.

Direct-Acting Oral Anticoagulants

Direct-acting oral anticoagulants (DOACs) have the advantage of more standardized dosing than warfarin without the need for regular INR monitoring. They also have minimal food and drug interactions in comparison.

The first DOAC, dabigatran, was approved in 2010. It works by directly inhibiting thrombin in the coagulation cascade. It is an oral drug used for the treatment of DVT (deep vein thrombosis)/PE (pulmonary embolism), stroke prevention in atrial fibrillation, and thromboembolism prophylaxis after hip arthroplasty. The capsules must be swallowed whole and cannot be crushed, opened, or chewed. It also must be stored in the original packaging and discarded four months after opening. It has a high risk of gastrointestinal side effects. When treating a DVT/PE, an initial period of parenteral anticoagulation is required before initiating dabigatran. The other DOACs are all selective factor Xa inhibitors. These drugs include apixaban, rivaroxaban, and edoxaban.

Apixaban is FDA approved to reduce stroke risk in clients with atrial fibrillation, to treat DVT/PE both acutely and to reduce the risk of recurrent thromboembolism after the initial treatment period, and for prevention of DVT after hip or knee replacement surgery. It is administered twice daily, whereas the other anti-Xa DOACs are administered only once daily. When treating atrial fibrillation, the dosing must be adjusted if the client meets certain thresholds based on renal function, age, and weight. When treating an acute DVT, a higher dose of apixaban is required for the first week of therapy.

Rivaroxaban is FDA approved for several thromboembolic-related indications. Some of the approved indications are reduction of stroke risk in clients with atrial fibrillation, stable coronary artery disease, treatment of DVT/PE, reduction of risk for recurrent DVT/PE, prophylaxis of DVT in clients undergoing hip or knee surgery, treatment of peripheral artery disease, and venous thromboembolism prophylaxis in acutely ill medical clients. For most indications, rivaroxaban must be taken with food to improve absorption.

Edoxaban is the newest anti-Xa DOAC, approved in 2015. It is FDA approved for stroke prevention in clients with atrial fibrillation and treatment of DVT/PE. When treating an acute DVT, an initial period of parenteral anticoagulation for 5–10 days is required before initiation of edoxaban. The most noteworthy aspects of edoxaban treatment are the renal considerations. Edoxaban carries a black box warning because it should not be used in clients with a creatinine clearance over 95 mL/min. It also should not be used in clients with severe renal dysfunction (creatinine clearance under 15 mL/min). Dose adjustments should be made based on moderate renal dysfunction or low body weight.

Table 20.2 lists common anticoagulants and typical routes and dosing for adult clients. Dose adjustments may be necessary for renal or hepatic impairment. Package inserts should be consulted accordingly.

Drug	Routes and Dosage Ranges
Heparin	Complicated and variable. Typical starting dose 18 units/kg/hr administered by continuous intravenous (IV) infusion, titrate to goal PTT or anti-Xa range. See Table 20.3 for sample heparin titration protocol. (Protocols are usually site specific and should be utilized accordingly.) *Venous prophylaxis of thromboembolism in acutely ill medical clients:* 5000 units subcutaneously every 8 hours.
Argatroban	Complicated and variable. Typical starting dose 2 mcg/kg/min administered as a continuous IV infusion, titrate to goal PTT. (Protocols are usually site specific and should be utilized accordingly.)
Bivalirudin (Angiomax)	*Treatment of heparin-induced thrombocytopenia (off-label):* Starting dose 0.15–0.20 mg/kg/hr as a continuous IV infusion, titrate to PTT goal.
Enoxaparin (Lovenox)	*Treatment of venous thromboembolism:* 1 mg/kg subcutaneously every 12 hours. *Venous thromboembolism prophylaxis in acutely ill medical clients:* 40 mg subcutaneously once daily.
Dalteparin (Fragmin)	*Treatment of deep vein thrombosis or pulmonary embolism:* 200 units/kg subcutaneously once daily or 100 units/kg subcutaneously twice daily.
Warfarin (Coumadin)	Complicated and variable. Dietary considerations for vitamin K content must be considered. Typical initial dose: 5 mg daily. Titrate to goal INR range (commonly 2–3).
Apixaban (Eliquis)	*Atrial fibrillation:* 5 mg orally twice daily. *Treatment of deep vein thrombosis or pulmonary embolism:* 10 mg orally twice daily for 7 days, followed by 5 mg twice daily.
Rivaroxaban (Xarelto)	*Atrial fibrillation:* 20 mg orally once daily with the evening meal. *Treatment of deep vein thrombosis or pulmonary embolism:* 15 mg orally twice daily with food for 21 days, followed by 20 mg once daily with food.

TABLE 20.2 **Drug Emphasis Table: Anticoagulants** (sources: https://dailymed.nlm.nih.gov/dailymed/; Linkins et al., 2012; Jaff et al., 2011)

Drug	Routes and Dosage Ranges
Edoxaban (Savaysa)	*Atrial fibrillation:* 60 mg orally once daily. *Treatment of deep vein thrombosis:* 60 mg orally once daily for clients >60 kg or 30 mg orally once daily for clients ≤60 kg (after at least 5 days of parenteral anticoagulation).
Dabigatran (Pradaxa)	*Atrial fibrillation:* 150 mg orally twice daily. *Treatment of deep vein thrombosis:* 150 mg orally twice daily (after at least 5 days of parenteral therapy).

TABLE 20.2 **Drug Emphasis Table: Anticoagulants** (sources: https://dailymed.nlm.nih.gov/dailymed/; Linkins et al., 2012; Jaff et al., 2011)

Anticoagulant Reversal Agents

Sometimes clients who have been administered anticoagulant medications experience serious bleeding complications or need urgent surgery that should not be performed while the blood is anticoagulated. In those cases, reversal agents may be administered to counteract the effect of the anticoagulant. The decision to administer a reversal agent is individualized and must consider the risk of continued bleeding (or potential surgical bleeding) as compared to the client's underlying thrombotic risk. The reversal agents do not work perfectly; they may not completely reverse the anticoagulant effect and additional risks may be present. This section will focus on protamine (reversal agent for heparins), vitamin K (reversal agent for warfarin), and monoclonal antibody reversal agents for the DOACs.

Protamine

Protamine is a protein that neutralizes heparin. It works via electrostatic interactions; it is a positively charged molecule that attracts and forms a salt with the negatively charged heparin molecules. Protamine has weak anticoagulant activity when given alone, but not when it forms a complex with heparin. Thus, dosing of protamine is important to neutralize the effect of heparin without allowing excess protamine to exert its anticoagulant effect. It is FDA approved to treat heparin overdose and is used off-label to partially neutralize low molecular weight heparins. An example of when this might be used is a client who has an intracranial hemorrhage and who cannot wait for the effect of heparin to wear off over time.

! SAFETY ALERT

Protamine

Protamine is administered by *slow* IV push, no faster than 50 mg per 10 minutes, because faster infusion causes hypotension. It also can cause severe hypersensitivity reactions, so the nurse should have resuscitation equipment and epinephrine available during administration for potential emergency response. The nurse should also monitor for heparin rebound, which can occur several hours later (typically 8–9 hours but can be as long as 18 hours later). Checking a PTT or anti-Xa level can help to monitor for this potential complication.

Vitamin K (Phytonadione)

Vitamin K is also known as phytonadione. It is the same substance present in food and is an antidote for the effect of warfarin. It is FDA approved for the reversal of anticoagulation due to warfarin, vitamin K deficiency, and for prophylaxis and treatment of vitamin K deficiency–related bleeding in newborns. It is available in oral and intravenous forms. The dose given and route of administration varies based on clinical need. Intravenous vitamin K reverses the effect of warfarin faster than oral vitamin K (onset within 1–2 hours vs. 6–10 hours) and is used during acute bleeding if urgent reversal is needed. When reversing the effect of warfarin, a higher dose is generally used for higher INR elevations. However, high doses can lead to difficulty anticoagulating a client with warfarin in the future. It is important to avoid confusion of vitamin K with potassium, which can also be abbreviated with "K."

DOAC Reversal Agents

Specific agents for DOAC reversal have been approved. Idarucizumab is used for life-threatening or uncontrolled bleeding in clients that have taken dabigatran. It is a humanized monoclonal antibody that binds dabigatran to remove it from the blood, ceasing its anticoagulant effect. Andexanet alfa is used for life-threatening or uncontrolled bleeding in clients who have taken apixaban or rivaroxaban. It is a recombinant inactive form of factor Xa. It binds

the factor Xa inhibitors, ceasing their anticoagulant effect. Prothrombin complex concentrates, which are the components of blood containing clotting factors, are also used for reversal of DOACs at some institutions.

Adverse Effects and Contraindications

The major side effect of all anticoagulant medications is bleeding complications. This can manifest in many different ways, including excessive bleeding in response to trauma or during surgery, gastrointestinal bleeding, or spontaneous intracranial hemorrhage. Some symptoms of bleeding are blood in the stool; dark, tarry-appearing stools; blood in the urine; epistaxis (nosebleed); gingival bleeding; very severe headache; coffee-ground emesis; and hemoptysis.

A history of bleeding complications such as intracranial hemorrhage or gastrointestinal bleeding may be considered a contraindication to further anticoagulant therapy. Concomitant medications that further increase bleeding risk, such as non-steroidal anti-inflammatory drugs (e.g., ibuprofen and naproxen) or antiplatelet agents (e.g. aspirin, discussed later in this chapter) should also be avoided with anticoagulants when possible. However, since anticoagulants treat life-threatening diseases, contraindications must be carefully considered. The risks and benefits of avoiding an anticoagulant due to a relative contraindication must be carefully weighed in the context of the risk of their primary disease state. For example, clients who have experienced multiple embolic strokes may still need anticoagulant therapy despite experiencing bleeding complications. For those clients, a lower intensity of anticoagulation or increased monitoring may be utilized to mitigate bleeding risk and balance risks/benefits. A client who has atrial fibrillation and a recent stent placed may need concomitant anticoagulant and antiplatelet medications, although it increases the risk of bleeding.

Table 20.3 is a drug prototype table for anticoagulants featuring warfarin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anticoagulant **Mechanism of Action** Inhibits the production of vitamin K, which is needed for synthesis of clotting factors II, VII, IX, and X	**Drug Dosage** Complicated and variable. Dietary considerations for vitamin K content must be considered. Typical initial dose: 5 mg daily. Titrate to goal INR range (commonly 2–3).
Indications Prophylaxis and treatment of venous thromboembolism and pulmonary embolism Prophylaxis and treatment of thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement Reduction in the risk of death, recurrent myocardial infarction (MI), and thromboembolic events such as stroke or systemic embolism after myocardial infarction **Therapeutic Effects** Anticoagulates the blood; increases INR to "thin" the blood	**Drug Interactions** Many drugs that interact through effects on metabolism by cytochrome P450 enzymes (e.g., amiodarone, rifampin) Many drugs that further increase bleeding risk (e.g., non-steroidal anti-inflammatory drugs, antiplatelet drugs) Many antibiotics and antifungals Many herbal products (e.g., St. John's wort, ginseng, garlic, ginkgo biloba) Recommended to consult a pharmacist for evaluation of drug interactions with warfarin **Food Interactions** Foods that contain vitamin K (e.g., spinach, kale, broccoli) Grapefruit juice Alcohol
Adverse Effects Bleeding, sometimes fatal hemorrhaging Tissue necrosis Systemic atheroemboli and cholesterol microemboli Hypersensitivity/allergic reactions Vasculitis Hepatitis, elevated liver enzymes Nausea, vomiting, taste perversion Rash, dermatitis, pruritis, alopecia	**Contraindications** Hypersensitivity Pregnancy, except with mechanical heart valves Hemorrhagic tendencies or blood dyscrasias Recent or contemplated surgery of the central nervous system or eye, or traumatic surgery resulting in large open surfaces Caution: Do not use as initial therapy in clients with acute HIT until after platelets recover

TABLE 20.3 **Drug Prototype Table: Warfarin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking anticoagulants:

- Monitor the drug effect via PTT, anti-Xa level, INR, or ACT depending on the specific anticoagulant use, as ordered by the provider or per the institutional protocol.
- Monitor the client for bleeding via decreases in hemoglobin and/or hematocrit and for other signs/symptoms; monitor platelets to identify bleeding risk.
- Familiarize themselves with institutional dosing protocols, especially any nurse-driven protocols.
- Utilize independent double checks for dose adjustments, especially heparin.
- Administer warfarin at the same time each day according to institutional policies.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an anticoagulant should:

- Recognize the signs and symptoms of bleeding as described under adverse effects and notify providers immediately if any of these signs or symptoms occur.
- Differentiate signs of typical bleeding, such as minor bruising, from signs of dangerous bleeding as described above.
- Recognize the signs and symptoms of therapeutic failure, depending on the disease state being treated.
- Avoid high-risk behaviors that could result in falls (such as working on rooftops or on tall ladders); injuries, especially head injuries, may be more severe in clients who take anticoagulants.
- Wear medical identification, such as a medical alert bracelet, so that if there is an emergency, providers are aware of the client's propensity to bleed.
- Avoid injecting through clothing or into skin that is bruised or scarred.
- Avoid ejecting the air bubble from the syringe.
- Avoid rubbing the injection site after administration.

FDA BLACK BOX WARNING

Enoxaparin, Dalteparin, Apixaban, Rivaroxaban, Edoxaban, Dabigatran

There is a risk for epidural or spinal hematomas in clients who take these anticoagulants and are undergoing spinal puncture or receiving neuraxial anesthesia. These can be very serious and result in long-term or permanent paralysis. These risks should be considered when scheduling clients for spinal procedures.

Warfarin

Warfarin can cause major or fatal bleeding. INRs should be monitored in all treated clients. Drugs, dietary changes, or other factors can affect INR levels. Instruct clients to minimize bleeding risk and report signs and symptoms to their provider.

Apixaban, Rivaroxaban, Edoxaban, Dabigatran

Premature discontinuation of these drugs can lead to increased risk of thrombotic events. Consider coverage with another anticoagulant if discontinued for reasons other than pathological bleeding or completion of therapy.

Edoxaban

Edoxaban should not be used in clients with creatinine clearance (CrCl) over 95 mL/min due to a higher rate of ischemic stroke in clients with atrial fibrillation. Another anticoagulant should be used.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Thomas Schmidt, a 48-year-old client, presents to the emergency department with reports of stabbing chest pain and is diagnosed with pulmonary embolism using computed tomography pulmonary angiography. Thomas is started on heparin. He is given an initial dose of 80 units/kg IV as a bolus, then started on a continuous infusion of 18 units/kg/hour.

History
Diabetes mellitus type 2

Current Medications
Metformin 500 mg orally daily

Vital Signs		Physical Examination
Temperature:	98.6°F	• *Head, eyes, ears, nose, throat (HEENT):* Denies any changes in vision. No difficulty hearing conversations. • *Cardiovascular:* No jugular vein distention or pedal edema noted; S1, S2 heard on auscultation. Denies chest pain. Capillary refill brisk, mucous membranes pink and moist. • *Respiratory:* Lungs clear to auscultation. Describes 8/10 stabbing chest pain. • *GI:* Abdomen soft, nontender, nondistended; bowel sounds heard in all four quadrants. No report of nausea, vomiting, or abdominal pain. Has regular daily bowel movements. • *GU:* Deferred. • *Neurological:* Alert and oriented to time, place, person, and events. • No reports of numbness, dizziness, vertigo, weakness, or seizures. • *Integumentary:* No wounds noted; skin appropriate for age.
Blood pressure:	125/85 mm Hg	
Heart rate:	90 beats/min	
Oxygen saturation:	98% on room air	
Height:	5'10"	
Weight:	253 lb	

TABLE 20.4

1. After 6 hours, a PTT is checked and the result is 75 seconds. Using the sample algorithm in Table 20.2, how will the nurse adjust the dose?
   a. 80 units/kg bolus, then increase rate by 4 units/kg/hr; recheck in 6 hours
   b. 40 units/kg bolus, then increase rate by 2 units/kg/hr; recheck in 6 hours
   c. Decrease infusion rate by 2 units/kg/hr; recheck in 6 hours
   d. Interrupt infusion for 1 hour, then decrease infusion rate by 3 units/kg/hr; recheck in 6 hours

2. The nurse is providing discharge teaching for Thomas, who will use low molecular weight heparin (LMWH) injections at home. Which of the following statements about LMWH therapy will the nurse include in the teaching plan?
   a. More frequent lab assessments are required with LMWH therapy.
   b. The duration of action is 2–4 times longer than heparin.
   c. The risks for bleeding are less.
   d. LMWH is more likely to cause thrombocytopenia.

20.3 Antiplatelets

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 20.3.1 Identify the characteristics of the antiplatelet drugs used to treat thrombus formation.
- 20.3.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of antiplatelet drugs used to treat thrombus formation.
- 20.3.3 Describe nursing implications of antiplatelet drugs used to treat thrombus formation.
- 20.3.4 Explain the client education related to antiplatelet drugs used to treat thrombus formation.

Antiplatelet drugs work by decreasing platelet activation and/or platelet adhesion. They are used for various indications including prevention and treatment of cardiovascular disease and prevention of ischemic stroke. One of the most common uses for antiplatelets is therapy after a client has an acute coronary syndrome and/or a coronary artery stent placed.

Antiplatelet Drugs

There are many antiplatelet drugs available. They will be discussed as grouped by mechanism of action.

Aspirin

Aspirin is an over-the-counter antiplatelet agent used for many indications. Some of those indications are secondary prevention of stroke, coronary artery disease, acute coronary syndromes, primary prevention of cardiovascular disease, peripheral artery disease, and prevention of thromboembolism in clients with certain heart valves. It also has anti-inflammatory and analgesic properties, which allow it to be used for pain, inflammatory conditions, and fever. Aspirin works as an antiplatelet agent by inhibiting the cyclooxygenase enzyme in platelets, which is responsible for production of prostaglandin precursors of thromboxane A2. Thromboxane A2 is a substance that activates platelets. Aspirin should not be routinely used in pediatric clients due to the risk of Reye syndrome. Like all antiplatelet agents, bleeding is a concerning side effect. However, in addition to the effect on platelets, aspirin can also increase the risk of gastric ulcer formation through inhibition of gastric prostaglandin synthesis. Subsequently, gastrointestinal effects are a major adverse effect, and it has additive gastrointestinal bleeding risk beyond its antiplatelet effect.

CLINICAL TIP

Chew Aspirin for Faster Absorption

If acute effects of aspirin are needed, such as during a heart attack, it is recommended that aspirin be chewed and swallowed for faster absorption (Mayo Clinic, n.d.).

P2Y12 Inhibitors

P2Y12 inhibitors are potent antiplatelet agents that work as antagonists at the P2Y12 subunit of the ADP receptor on the platelet surface, which decreases platelet activation at the site of vessel injury. Because of their effect on bleeding, it is recommended that P2Y12 inhibitors be discontinued 5–7 days prior to surgery, depending on the agent. There are currently four P2Y12 inhibitors available in the United States: clopidogrel, prasugrel, ticagrelor, and cangrelor. P2Y12 inhibitors require a loading dose if immediate therapeutic effect is needed (e.g., in an acute myocardial infarction). Onset is slower without loading doses.

Clopidogrel is a prodrug, meaning it must be metabolized to become biologically active. This activation is accomplished through the enzyme CYP2C19. This is significant because clients can have a genetic alteration in this enzyme that inhibits clopidogrel activation, which could lead to therapeutic failure. It is also important because it confers drug interactions. If clients without any genetic alteration take a concomitant drug that inhibits CYP2C19, the enzyme will not be available to activate clopidogrel, which could lead to therapeutic failure.

SAFETY ALERT

Clopidogrel

Clopidogrel requires a loading dose if immediate onset is desired, such as during an acute coronary syndrome. Initiating clopidogrel without a loading dose will result in a delayed effect up to several days, putting the client at risk for a thromboembolic event.

Ticagrelor and prasugrel are two additional oral P2Y12 inhibitors that are stronger in their antiplatelet effect compared to clopidogrel. Prasugrel is a prodrug that must be activated in the body, but it does not rely on CYP2C19 for activation, so it is less susceptible to drug interactions or therapeutic failure due to genetics. However, prasugrel has a comparatively higher risk of bleeding and the highest risk of fatal bleeding of these agents. It is also contraindicated in clients with a history of a stroke or transient ischemic attack, clients who are older than 75 years of age unless they are at very high risk of thromboembolism, and clients who weigh less than 60 kg.

Ticagrelor does not require activation, so like prasugrel, it is not susceptible to CYP2C19-mediated drug interactions or genetic polymorphisms. A noteworthy side effect of ticagrelor is dyspnea, which can limit activities of daily living. It also has a boxed warning from the FDA regarding concomitant aspirin doses, which should not exceed 100 mg orally per day. It is contraindicated in clients with a history of intracranial hemorrhage.

Cangrelor is the only intravenous P2Y12 inhibitor. It is approved for use during percutaneous coronary intervention. The advantage of cangrelor is that it inhibits platelets nearly immediately upon administration, and platelet function

recovers within an hour of medication discontinuation.

Eptifibatide

Eptifibatide inhibits the GPIIbIIIa receptor on the platelet surface, preventing activation by von Willebrand's factor and fibrinogen. This receptor is responsible for the final step in platelet-to-platelet adhesion; thus, this is a very potent antiplatelet agent. It is FDA approved for use during percutaneous coronary intervention in clients experiencing a non-ST-elevation acute coronary syndrome. The major side effect of eptifibatide is profound thrombocytopenia. Nurses should monitor the client's platelet count closely and discontinue eptifibatide if the platelet count decreases to under 100,000/mm^3.

Table 20.5 lists common antiplatelets and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Aspirin	*Typical maintenance dose for ischemic heart disease:* 81 mg orally daily (often referred to as low-dose or "baby" aspirin). *Acute myocardial infarction:* 325 mg orally once for aspirin-naïve clients experiencing acute myocardial infarction.
Clopidogrel (Plavix)	*Maintenance dose for ischemic heart disease:* 75 mg orally daily.
Prasugrel (Effient)	*Maintenance dose for ischemic heart disease:* *Clients ≥60 kg:* 10 mg orally once daily. *Clients <60 kg:* 5 mg orally once daily.
Ticagrelor (Brilinta)	*Typical maintenance dose for ischemic heart disease:* 90 mg orally twice daily.
Cangrelor (Kengreal)	*Antiplatelet agent during percutaneous coronary intervention:* 30 mcg/kg IV bolus followed by 4 mcg/kg/min IV infusion.
Eptifibatide (Integrelin)	*Acute coronary syndrome or percutaneous coronary intervention (PCI):* 180 mcg/kg IV bolus followed by 2 mcg/kg/min IV infusion. (For PCI, add a second 180 mcg/kg bolus at 10 minutes.)

TABLE 20.5 Drug Emphasis Table: Antiplatelets (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Like anticoagulants, the major side effect of all antiplatelet medications is bleeding complications. This can manifest in many different ways, including excessive bleeding in response to trauma or during surgery, gastrointestinal bleeding, or spontaneous intracranial hemorrhage. Some symptoms of bleeding are blood in the stool; dark, tarry-appearing stools; blood in the urine; epistaxis; gingival bleeding; very severe headache; coffee-ground emesis; and hemoptysis.

A history of bleeding complications, such as intracranial hemorrhage or gastrointestinal bleeding, may be considered a contraindication to further antiplatelet therapy, depending on the circumstances and the drug. Concomitant medications that further increase bleeding risk such as non-steroidal anti-inflammatory drugs (e.g., ibuprofen and naproxen) or antiplatelet agents (e.g., aspirin) may also be considered contraindicated with antiplatelet medications.

Table 20.6 is a drug prototype table for antiplatelet agents featuring clopidogrel. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antiplatelet agent; P2Y12 inhibitor **Mechanism of Action** Inhibits platelet activation through binding to the P2Y12 class of ADP receptors on platelets	**Drug Dosage** *Maintenance dose for ischemic heart disease:* 75 mg orally daily.
Indications Acute coronary syndromes To reduce the rate of myocardial infarction and stroke in clients with recent myocardial infarction, stroke, or established peripheral artery disease **Therapeutic Effects** Decreases platelet activation Decreases clotting risk	**Drug Interactions** CYP2C19 inhibitors Opioids NSAIDs, warfarin, SSRIs, SNRIs Other antiplatelet or anticoagulant agents Repaglinide **Food Interactions** Grapefruit juice*
Adverse Effects Bleeding Life-threatening bleeding Fatal bleeding	**Contraindications** Hypersensitivity Active pathological bleeding, such as peptic ulcer or intracranial hemorrhage Caution: Premature discontinuation increases risk of cardiovascular events Thrombocytopenic purpura has been reported

TABLE 20.6 **Drug Prototype Table: Clopidogrel** (sources: https://dailymed.nlm.nih.gov/dailymed/; *Holmberg et al., 2014)

Nursing Implications

The nurse should do the following for clients who are taking antiplatelets:

- Monitor the client for bleeding via a complete blood count and monitoring for other signs/symptoms.
- Monitor the client for bleeding via decreases in hemoglobin and/or hematocrit and monitoring for other signs/symptoms; monitor platelets to identify bleeding risk.
- Pay special attention to dosing; initial doses of antiplatelet medications may be higher as a single loading dose to accelerate the onset of effect.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antiplatelet drug should:

- Recognize the signs and symptoms of bleeding as described under adverse effects. Providers should be notified immediately if any of these signs and symptoms occur.
- Recognize the signs and symptoms of therapeutic failure, depending on the disease state being treated.
- Avoid high-risk behaviors that could result in falls (such as working on rooftops or on tall ladders). Clients must be educated that injuries, especially head injuries, may be more severe in clients who take antiplatelets.
- Wear medical identification, such as a medical alert bracelet, so that if there is an emergency, their providers are aware of the client's propensity to bleed.

FDA BLACK BOX WARNING

Clopidogrel

The antiplatelet effect of clopidogrel is diminished in clients with two loss-of-function alleles of the CYP2C19 gene. Consider use of another platelet P2Y12 inhibitor in clients identified as CYP2C19 poor metabolizers.

Ticagrelor

Ticagrelor can cause significant and sometimes fatal bleeding. It should be avoided in clients with active pathological bleeding or a history of intracranial hemorrhage. It should not be started in clients undergoing urgent coronary artery bypass graft surgery. If possible, manage bleeding without discontinuing ticagrelor since discontinuation will increase the risk of subsequent cardiovascular events. Ticagrelor also has a boxed warning stating that the maintenance dose of aspirin over 100 mg daily reduces the effectiveness of ticagrelor and should be avoided.

Prasugrel

Prasugrel can cause significant and sometimes fatal bleeding. It should not be used in clients with active pathological bleeding or a history of transient ischemic attack or stroke. It is generally not recommended in clients 75 years old or older unless the client is at particularly high risk. Do not start prasugrel in clients likely to undergo urgent coronary artery bypass grafting, and discontinue at least 7 days prior to any surgery. If possible, manage bleeding without discontinuing prasugrel, as discontinuation increases the risk of subsequent cardiovascular events.

20.4 Thrombolytics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 20.4.1 Identify the characteristics of the thrombolytic drugs used to treat thrombus formation.
- 20.4.2 Explain the indications, actions, adverse reactions, and interactions of the thrombolytic drugs used to treat thrombus formation.
- 20.4.3 Describe nursing implications of thrombolytic drugs used to treat thrombus formation.
- 20.4.4 Explain the client education related to thrombolytic drugs used to treat thrombus formation.

Thrombolytics to Break Down an Existing Clot

Anticoagulant and antiplatelet medications work in the clotting cascade to prevent clotting in clients without a thromboembolism or to prevent worsening of an existing clot while the body breaks the clot down over time. Conversely, thrombolytics work to quickly break down an existing clot, which is often needed when the clot is blocking blood flow to a major organ. They work by facilitating conversion of plasminogen to plasmin. Plasmin then initiates fibrinolysis, or fibrin clot breakdown.

SAFETY ALERT

Alteplase

Alteplase is frequently referred to as tPA as an abbreviation for tissue plasminogen activator (which refers to the mechanism of action). However, this can be confused with TNK, an abbreviation sometimes used for tenecteplase, or TPN, the abbreviation for total parenteral nutrition, which has led to medication errors and/or medication delays in circumstances where timing is crucial. The nurse should avoid using tPA as an abbreviation for alteplase.

See this Institute for Safe Medication Practices (ISMP) report for more information on potential medication errors associated with alteplase (https://openstax.org/r/confusion).

Alteplase

Alteplase is an intravenous thrombolytic drug that is approved to treat acute ischemic stroke, acute myocardial infarction, and pulmonary embolism. Alteplase works quickly upon administration, and the half-life is less than 5 minutes. It requires reconstitution prior to administration, which is somewhat complicated and further explained in the product labeling and manufacturer website (https://openstax.org/r/activase). Because of the high risk of bleeding, the risks and benefits must be carefully weighed prior to administration. Alteplase has many contraindications, which are listed in Table 20.8. These contraindications are clinical characteristics or disease states that put the client at an unacceptable risk for bleeding complications. For example, severe uncontrolled hypertension increases the risk of intracranial hemorrhage in clients receiving alteplase. Thus, alteplase should be avoided in those clients. Prior to administering alteplase, the nurse should confirm that the client does not have any contraindications to therapy.

In small doses, alteplase can also be used as an agent to restore function of central venous access devices that are unable to draw blood due to thrombus formation. For this use, it is known by the brand name Cathflo Activase.

Tenecteplase

Tenecteplase is approved for treatment of ST-elevation myocardial infarction (STEMI). The most common adverse effects are bleeding and hypersensitivity. Like alteplase, it has many contraindications that would put the client at an unacceptable risk of bleeding: active internal bleeding, history of cerebrovascular accident, intracranial or intraspinal surgery or trauma within 2 months, intracranial neoplasm, arteriovenous malformation, or aneurysm, known bleeding diathesis, and severe uncontrolled hypertension. Although not FDA approved, off-label use of tenecteplase for acute ischemic stroke is gaining popularity and is listed as an option in the guidelines for treatment of acute ischemic stroke (Powers, 2019). Some of the practical advantages of tenecteplase as compared to alteplase are that it is quicker to prepare, does not require a dedicated intravenous line or pump, and can be administered as an IV bolus.

Table 20.7 lists common thrombolytics and typical routes and dosing for adult clients. Protocols are usually site specific and should be utilized accordingly.

Drug	Routes and Dosage Ranges
Alteplase (Activase, Cathflo Activase)	*Acute ischemic stroke:* 0.9 mg/kg (not to exceed 90 mg total) IV over 60 minutes, with 10% of the dose administered as an initial bolus over 1 minute. *Acute myocardial infarction:* Weight-based dosing up to maximum of 100 mg. *Acute massive pulmonary embolism:* 100 mg IV infusion over 2 hours. *Restoration of function of central venous access devices (Cathflo Activase):* Instill 2 mg/2 mL into the dysfunctional catheter.
Tenecteplase (TNKase)	*Acute ST elevation myocardial infarction:* Weight-based dosing; 30–50 mg administered as a single IV bolus based on the client's weight. *Acute-ischemic stroke (off-label)*:* 0.25 mg/kg IV; maximum dose: 25 mg.

TABLE 20.7 Drug Emphasis Table: Thrombolytics (sources: https://dailymed.nlm.nih.gov/dailymed/; *Powers et al., 2019)

Adverse Effects and Contraindications

The main adverse effect of thrombolytic therapy is bleeding, which is sometimes severe and can be fatal. This is especially frequent at arterial and venous puncture sites, which leads to nursing implications regarding vascular access described in the next section. Hypersensitivity reactions are also possible. When used to treat coronary thrombus in a client with an acute myocardial infarction, there is an increased risk of dysrhythmias after blood flow is restored. The specific contraindications to thrombolytics are discussed within the content for the specific drugs but are mostly related to bleeding risk.

Table 20.8 is a drug prototype table for thrombolytics featuring alteplase. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Thrombolytic **Mechanism of Action** Converts plasminogen to plasmin, which breaks down clot-bound fibrin	**Drug Dosage** *Acute ischemic stroke:* 0.9 mg/kg (not to exceed 90 mg total) IV over 60 minutes, with 10% of the dose administered as an initial bolus over 1 minute. *Acute myocardial infarction:* Weight-based dosing up to maximum of 100 mg. *Acute massive pulmonary embolism:* 100 mg IV infusion over 2 hours. *Restoration of function of central venous access devices (Cathflo Activase):* Instill 2 mg/2 mL into the dysfunctional catheter.
Indications Acute ischemic stroke Acute myocardial infarction Acute massive pulmonary embolism **Therapeutic Effects** Breaks down thrombus to restore blood flow	**Drug Interactions** Anticoagulants Antiplatelets ACE inhibitors **Food Interactions** No significant interactions
Adverse Effects Bleeding, including severe bleeding and fatal bleeding	**Contraindications** *General:* Active internal bleeding Recent intracranial or intraspinal surgery or serious head trauma Intracranial conditions that may increase risks for bleeding Current severe uncontrolled hypertension *Acute ischemic stroke:* Current intracranial hemorrhage Subarachnoid hemorrhage *Acute myocardial infarction or pulmonary embolism:* History of recent stroke Caution: Increased risk for bleeding Monitor for hypersensitivity Reembolization risk from lysis of DVT Cholesterol embolism (rare)

TABLE 20.8 **Drug Prototype Table: Alteplase** (sources: https://dailymed.nlm.nih.gov/dailymed/; *Powers et al., 2019)

Nursing Implications

The nurse should do the following for clients who are taking thrombolytics:

- Obtain baseline vital signs.
- Avoid intramuscular injections, internal jugular, and subclavian venous punctures during infusion. If an arterial puncture is necessary during infusion, the nurse should use an upper extremity blood vessel that can be compressed and should apply pressure applied for 30 minutes afterward. The nurse should also monitor the puncture site closely.
- Ensure clients remain on bedrest following thrombolytic administration to reduce falls and subsequent bleeding risk.
- Monitor the client for bleeding via a complete blood count and monitoring for other signs/symptoms.
- Notify the provider immediately if signs or symptoms of bleeding occur; treatments such as cryoprecipitate

(blood-derived clotting factors) or antifibrinolytic medications (medications that prevent fibrin breakdown, such as aminocaproic acid or tranexamic acid) may be warranted.
- Monitor for hypersensitivity reactions.
- Initiate an additional IV line for clients receiving alteplase because alteplase requires a dedicated IV line.
- Monitor for changes in the client's condition depending on the indication for use.
- Administer thrombolytic therapy promptly; there are specific time frames that the drug must be administered for full therapeutic effect, depending on the disease state being treated.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a thrombolytic should:

- Recognize the signs/symptoms of bleeding as described under adverse effects. Providers should be notified immediately if any of these signs and symptoms occur.
- Recognize the signs/symptoms of therapeutic failure, depending on the disease state being treated.
- Remain on bedrest after thrombolytic administration to reduce falls and subsequent bleeding risk.
- Follow drug-specific dietary guidelines.

The client taking a thrombolytic *should not:*

- Discontinue therapy unless following specific instructions from the health care provider.
- Schedule any invasive procedure without direct communication with the health care provider, including but not limited to dental procedures.

Chapter Summary

This chapter described the physiology of forming a blood clot, including review of the coagulation cascade and platelet activation. It examined the various medications for prevention and treatment of thromboembolism. Anticoagulant mediations were summarized, including both injectable and oral forms. Special attention was paid to client education on warfarin therapy and enoxaparin injection technique. Antiplatelet medications were also described. Finally, thrombolytics were discussed. Bleeding risk was central to the discussion of each of these classes of medications.

Key Terms

activated clotting time (ACT) a way to measure the time it takes to form a clot; available as a point-of-care test

anti-factor Xa level (anti-Xa) measurement of the concentration of drugs that inhibit factor Xa in the clotting cascade

anticoagulants drugs that work in different parts of the coagulation cascade to decrease the propensity of the blood to form a clot

clotting factors proteins that work to activate different parts of the coagulation cascade

coagulation cascade series of events that leads to blood clotting

complete blood count laboratory blood test that measures the amount of red blood cells, white blood cells, hemoglobin, hematocrit, and platelets

deep vein thrombosis (DVT) blood clot that forms in a vein

erythrocytes red blood cells

fibrinolysis breakdown of fibrin

hematocrit percentage or proportion of red blood cells in the blood

hemoglobin substance that binds oxygen and facilitates oxygen transport in the blood

hemostasis the ability to cease bleeding

heparin-induced thrombocytopenia (HIT) major complication of heparin therapy characterized by a decrease in platelets and concomitant hypercoagulable state

hypercoagulable excessive propensity to form a clot

international normalized ratio provides another measurement of the length of time the blood takes to clot, calculated using the prothrombin time (PT)

ischemic stroke when a clot obstructs blood flow to the brain

partial thromboplastin time (PTT) laboratory test obtained via venous blood sample that provides a measurement of the length of time the blood takes to clot

platelets component of the blood that bind together and to endothelial tissue to form a clot

prothrombin time (PT) a measurement of the time it takes to form a clot; used to calculate the international normalized ratio (INR)

pulmonary embolism (PE) a clot that has typically formed in a vein but has broken off and lodged in the vasculature of the lungs

thrombolytics drugs that dissolve existing clots

thrombosis the formation of a clot that obstructs blood flow

Review Questions

1. The nurse admits a client with an acute pulmonary embolism and is instructed to start heparin. Which of the following tests can the nurse best use to adjust the dose of heparin?
   a. Partial thromboplastin time (PTT)
   b. International normalized ratio (INR)
   c. Complete blood count (CBC)
   d. Prothrombin time (PT)

2. A client who received heparin developed uncontrollable bleeding. What medication is the provider most likely to use as an antidote to the heparin?
   a. Protamine
   b. Phytonadione
   c. Idarucizumab
   d. Andexanet alfa

3. The nurse is answering the client's question about the risk for heparin-induced thrombocytopenia (HIT). Which of the following information should be included in the discussion?

a. The condition increases the risk for bleeding.
b. The platelet count rises above normal initially.
c. The condition is immune mediated.
d. The skin rash is the most reliable diagnostic indicator.

4. A client is admitted to the emergency department with an acute myocardial infarction. Which medication does the nurse anticipate being ordered to dissolve the clot in the coronary artery?
a. Vitamin K
b. Alteplase
c. Warfarin
d. Enoxaparin

5. The nurse is teaching a client with a pulmonary embolism about their new medication, heparin. What will the nurse tell the client about the purpose of heparin?
a. It will dissolve the blood clot quickly.
b. It will prevent platelet-to-platelet adhesion.
c. It will enhance clotting.
d. It will prevent further clot formation.

6. A nurse is teaching a client about warfarin dietary considerations. Which of the following statements by the client indicates understanding of the restrictions?
a. "I should eat a lot of spinach every day due to increased vitamin K needs."
b. "I can eat a lot of extra broccoli with a meal as long as it is only occasionally due to decreased vitamin K needs."
c. "I should avoid eating fruit like bananas due to excess vitamin K content."
d. "I should eat a consistent amount of vitamin K–containing foods in my diet."

7. A nurse admits a client who has been started on warfarin for a pulmonary embolism. Which test will the nurse monitor to assess warfarin's effect?
a. Partial thromboplastin time (PTT)
b. International normalized ratio (INR)
c. Complete blood count (CBC)
d. Anti-factor Xa level

8. The nurse is monitoring for medication-related adverse effects in a client receiving heparin. Which of the following would indicate that the client should be assessed for heparin-induced thrombocytopenia (HIT)?
a. A decrease in platelet count and concomitant gastrointestinal bleed
b. A decrease in platelet count and concomitant deep vein thrombosis
c. An increase in platelet count and concomitant intracranial hemorrhage
d. An increase in platelet count and concomitant pulmonary embolism

9. Which of the following direct-acting oral anticoagulant drugs must be taken with food for effective absorption?
a. Endoxaban
b. Dabigatran
c. Rivaroxaban
d. Apixaban

10. An emergency department nurse is assessing a client with an acute ischemic stroke prior to administering alteplase. Which finding will the nurse need to discuss with the provider prior to administering alteplase therapy?
a. Total knee replacement surgery 6 months ago
b. Blood pressure of 197/110 mm Hg

c. Glucose level of 168 mg/dL
d. Past medical history of gastroesophageal reflux disease (GERD)

CHAPTER 21
Lipid-Lowering Drugs

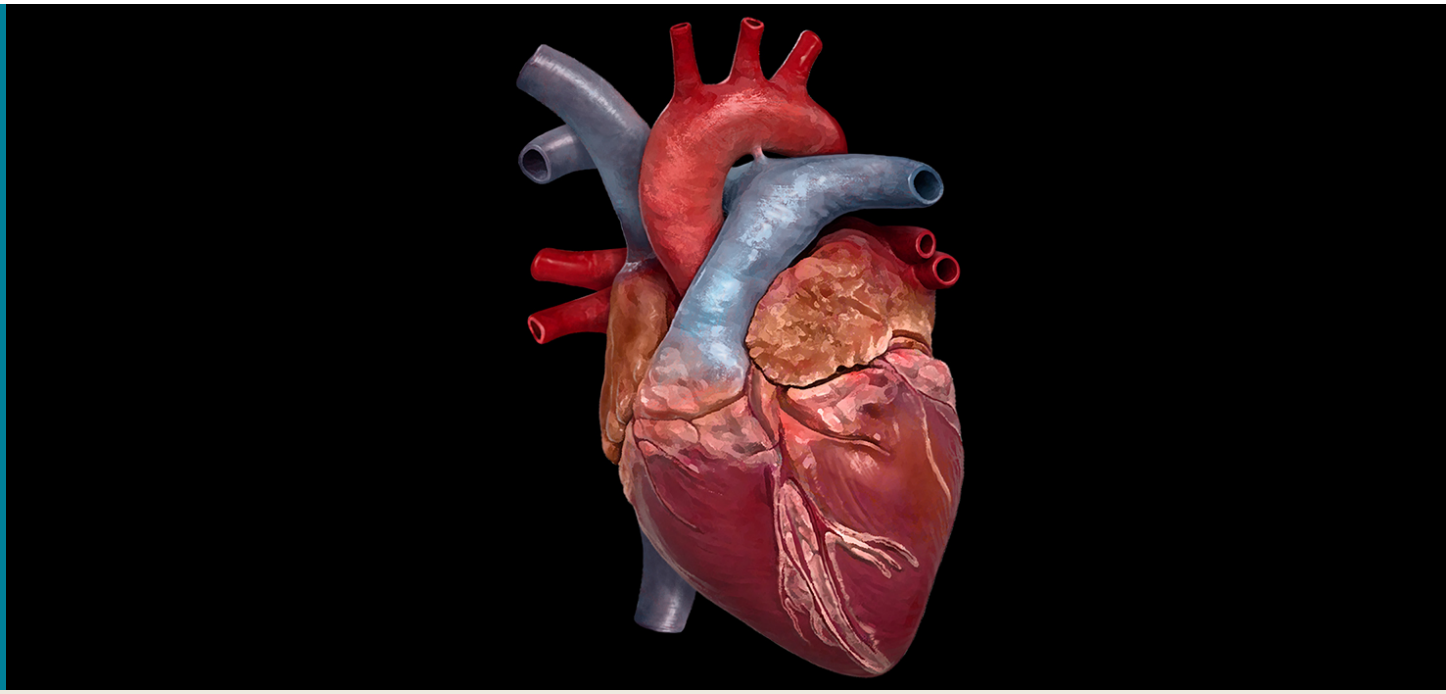


FIGURE 21.1 The heart is the primary organ of the cardiovascular system, controlling circulation and blood flow for the entire body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Lipids are fatty, waxy, or oily substances that have important roles in the body. Some of the most important ones are energy storage, regulation of body temperature, and hormonal regulation. Lipids are also an integral part of the cell membrane of each cell in the body. There are three types of lipids, which are differentiated by their chemical structure: triglycerides, sterols, and phospholipids. This chapter will focus on triglycerides and sterols and the drugs used to manage their elevations in the blood.

21.1 Introduction to Lipoprotein and Apolipoproteins

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 21.1.1 Discuss fat metabolism and the role of lipoproteins and apolipoproteins in the body.
- 21.1.2 Discuss the role of lipids as a risk factor for coronary artery disease.

Understanding Lipids

Triglycerides are the main dietary source of fat. They are composed of three long fatty acid chains attached to a glycerol backbone, as depicted in Figure 21.2. The major sterol in the body is cholesterol. **Cholesterol** is important for the structure of cell membranes and for the production of hormones, bile acids, and vitamin D.

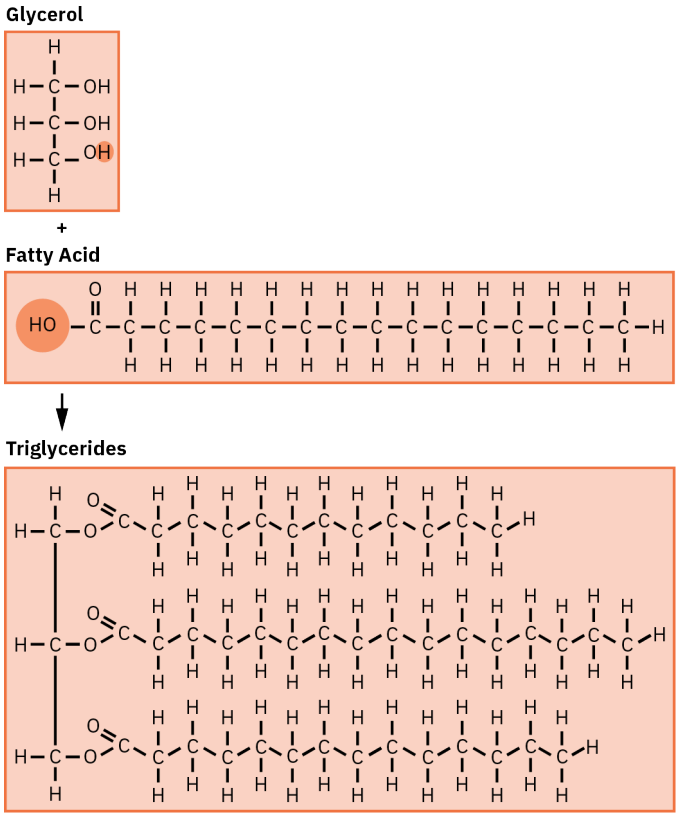


FIGURE 21.2 Triglycerides are composed of a glycerol backbone attached to three fatty acid chains. The fatty acids can be stored and released later for energy. (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Dyslipidemia is the general term to describe abnormal lipid levels or an imbalance of lipids in the blood. **Hyperlipidemia** refers to excessive serum levels of lipids. It can be categorized as **hypertriglyceridemia** (excessive triglycerides in the blood) or **hypercholesterolemia** (excessive cholesterol in the blood). Hypercholesterolemia is extremely prevalent, affecting 11.5%–38.1% of adults in the United States (Centers for Disease Control and Prevention, 2023b; Tsao et al., 2022). Many individuals with hypercholesterolemia have no symptoms; the diagnosis is made by monitoring their lipid panel. **Familial hypercholesterolemia** is a genetic disorder that manifests as very high cholesterol levels that can cause early cardiovascular disease. People with familial hypercholesterolemia can have one or two copies of the gene for familial hypercholesterolemia. Clients with one copy of the gene have heterozygous familial hypercholesterolemia, which is a mild form of the disease. Clients with two copies of the gene have homozygous familial hypercholesterolemia. This is a much more severe form of the disease and manifests during childhood. Some of the signs and symptoms of familial hypercholesterolemia are bumps or lumps around the knees, knuckles, or elbows; swollen or painful Achilles tendon; yellowish areas around the eyes; and a whitish-gray color in the shape of a half-moon on the outer edge of the cornea, which are lipid deposits called arcus senilis (Centers for Disease Control and Prevention, 2020).

LINK TO LEARNING

Cholesterol and Triglycerides

Access multimedia content (https://openstax.org/books/pharmacology/pages/21-1-introduction-to-lipoprotein-and-apolipoproteins)

This video from the American Heart Association introduces cholesterol and triglycerides. It gives an overview of the types of cholesterol particles and their associated cardiovascular risk.

Lipoproteins

Lipoproteins are combinations of lipids and proteins that carry cholesterol and triglycerides in the blood.

Chylomicrons are lipoproteins produced by enterocytes in the gut. They carry triglycerides to the tissues after dietary consumption. Three major types of lipoproteins are made by the liver. They vary in their relative amounts of triglycerides and cholesterol:

- **Very low-density lipoproteins (VLDL)**
- **Low-density lipoproteins (LDL or LDL-cholesterol)**
- **High-density lipoproteins (HDL or HDL-cholesterol)**

VLDL is predominantly composed of triglycerides, whereas LDL-cholesterol and HDL-cholesterol are richer in cholesterol. Triglycerides carried by VLDL and LDL-cholesterol are mediators of **atherosclerosis** development. Atherosclerosis refers to the formation of fatty material, called plaques, on inner arterial walls. It can lead to coronary artery disease, myocardial infarction, ischemic stroke, and peripheral artery disease. Therefore, LDL-cholesterol is often called "bad cholesterol." HDL-cholesterol, on the other hand, is often called "good cholesterol" because it does not contribute to atherosclerosis; in fact, it removes cholesterol from the blood (Grundy et al., 2019).

Lipid levels in the blood are monitored using a blood test called a lipid panel. A lipid panel measures LDL-cholesterol, HDL-cholesterol, and triglycerides. It also measures the total cholesterol level. In most cases, the LDL-cholesterol level on a lipid panel is calculated using the Friedewald formula, shown below (Friedewald, 1972). Note that all of the values must be measured in milligrams per deciliter (mg/dL).

$$\text{LDL Cholesterol} = \text{Total Cholesterol} - \text{HDL Cholesterol} - \frac{\text{Triglygerides}}{5}$$

Optimal levels of cholesterol are subject to debate and depend on individual characteristics and cardiovascular risk. However, generally accepted optimal cholesterol levels are shown in Table 21.1.

Lipid	Optimal Level
Total cholesterol	About 150 mg/dL
LDL-cholesterol	About 100 mg/dL
HDL-cholesterol	At least 40 mg/dL in males and 50 mg/dL in females
Triglycerides	Less than 150 mg/dL

TABLE 21.1 **Optimal Cholesterol Levels** (source: Centers for Disease Control and Prevention, 2023a)

Lipid Metabolism

Fats from the diet are emulsified by bile acids, which are made in the liver and secreted by the gallbladder when food is consumed. The emulsified fats are absorbed in the small intestine and carried via chylomicrons to the tissues. Chylomicrons interact with an enzyme called **lipoprotein lipase** on muscle and adipose tissue, thereby facilitating the release of free fatty acids from the triglycerides. The free fatty acids can be burned by the tissues for energy or stored as fat. The remnants of chylomicrons that are left over after fatty acid delivery return to the liver. Apolipoproteins A, B, C, and E are all involved in different aspects of this pathway.

The liver also synthesizes cholesterol and triglycerides. Cholesterol is synthesized via an enzyme called **HMG CoA reductase**, which is a key drug target in lipid-lowering therapy. The liver then packages cholesterol and triglycerides into VLDL particles, which travel to muscle and adipose tissue. Lipoprotein lipase breaks down VLDL particles to release free fatty acids from triglycerides for energy or storage. The remnants left over from the VLDL particles are called intermediate-density lipoproteins, which can be disposed of by the liver or further broken down by lipases to form LDL particles. LDL receptors in the liver interact with LDL-cholesterol to engulf it via endocytosis and dispose of it, effectively removing it from circulation. A protein called PCSK9 interacts with the LDL receptors, leading to their degradation; this is another important drug target in lipid-lowering therapy. HDL-cholesterol also assists in removing cholesterol from the circulation.

TRENDING TODAY

Ketogenic Diet

The ketogenic diet, often called "keto," was originally used to help children suffering from frequent seizures. However, it has recently become a popular diet for those seeking weight loss. The diet consists of very low amounts of carbohydrates and higher amounts of fat. When very low amounts of carbohydrates are consumed, the body uses ketone bodies, made from fats, as the major fuel instead of glucose. Although this diet can lead to rapid weight loss, it can be very difficult to sustain. A typical 2000-calorie ketogenic diet would limit carbohydrates to 20–50 g per day (Masood et al., 2022). A single apple could satisfy the entire daily intake of carbohydrate for a ketogenic diet. The keto diet also may be associated with increased lipid levels and cardiovascular disease.

Lipids and Coronary Artery Disease

Cholesterol has a central role in the development of coronary artery disease (CAD). CAD is characterized by plaque buildup within the coronary arteries, which can occlude blood flow to the heart muscle. The development of CAD starts with cholesterol and triglycerides, which can be deposited onto the inner walls of arteries. Cells from the immune system called macrophages engulf the cholesterol, forming foam cells and fatty streaks within the arterial wall. Over time, cells and cellular debris build up on the fatty streaks, and a fibrous cap forms to create plaques that can narrow the artery and obstruct blood flow. Rupture of the fibrous plaque can cause a thrombus, or blood clot, to form at the site, possibly resulting in complete arterial occlusion and acute myocardial infarction.

LINK TO LEARNING

Cholesterol and Coronary Artery Disease (https://openstax.org/r/watchlearnli)

This interactive slide presentation from the American Heart Association introduces the role of cholesterol in the pathophysiology of CAD.

Because of this pathophysiology, hypercholesterolemia due to elevated LDL-cholesterol is an independent risk factor for heart disease. Lipid-lowering therapy that targets LDL-cholesterol is used to decrease the risk for CAD. The optimal target levels for LDL-cholesterol and specific treatment strategies recommended in national guidelines have changed over the last 15 years and continue to evolve; however, the role of LDL-cholesterol as an independent risk factor has not changed.

Although triglycerides have been implicated in the development of atherosclerosis, treatment has not resulted in positive cardiovascular outcomes. Therefore, hypertriglyceridemia is generally not treated unless it is very severe (greater than 500 mg/dL), which can put the individual at risk for pancreatitis.

HDL-cholesterol actually has a protective role against cardiovascular disease, and higher levels (Table 21.1) are considered beneficial.

LINK TO LEARNING

Cholesterol Guidelines

Access multimedia content (https://openstax.org/books/pharmacology/pages/21-1-introduction-to-lipoprotein-and-apolipoproteins)
This video from JAMA Network gives a quick overview of cholesterol management according to the 2018 American College of Cardiology/American Heart Association guidelines. It provides some context on the changes from previous management recommendations.

In general, lifestyle changes are considered the first-line therapy to treat dyslipidemia and prevent CAD. Many therapeutic drugs are also available. These drugs are listed in Table 21.2 and are the focus of the remainder of the chapter.

Primary Target to Decrease*	Drug Classes or Drugs	Drug Mechanism
LDL-cholesterol	Ezetimibe	Decreases cholesterol absorption
	Statins Bempedoic acid	Decrease cholesterol synthesis
	PCSK9 inhibitors Inclisiran	Increase cholesterol removal
	Niacin	Multiple actions; not well understood
Triglycerides	Fibrates	Stimulate triglyceride breakdown
	Niacin	Multiple actions; not well understood
	Omega-3 fatty acids Icosapent ethyl	Thought to reduce hepatic production of VLDL
	Bile acid sequestrants	Divert cholesterol for bile acid production

TABLE 21.2 Summary of Lipid-Lowering Drugs (*Only the primary target is shown; other effects on lipid parameters are not listed.) (sources: Bornfeldt, 2021; https://dailymed.nlm.nih.gov/dailymed/)

CLINICAL TIP

Diet

A heart-healthy diet can help reduce cardiovascular risk and is the first-line therapy for cardiovascular risk reduction and hyperlipidemia.

Clients should eat:

- Vegetables
- Whole grains
- Legumes
- Healthy protein sources
- Nontropical vegetable oils

Clients should limit intake of:

- Sweets
- Sugar-sweetened beverages
- Red meats
- Saturated fats and trans fats
- Dairy products made from whole milk

(Sources: American Heart Association, 2020; Centers for Disease Control and Prevention, 2023b, 2023c; Grundy et al., 2019)

21.2 Statins (HMG-CoA Reductase Inhibitors) and PCSK9 Inhibitors

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 21.2.1 Identify the characteristics of statins (HMG-CoA reductase inhibitors) and PCSK9 inhibitor drugs used to lower lipid levels.
- 21.2.2 Explain the indications, action, adverse reactions, and interactions of statins (HMG-CoA reductase inhibitors) and PCSK9 inhibitor drugs used to lower lipid levels.
- 21.2.3 Describe nursing implications of statins (HMG-CoA reductase inhibitors) and PCSK9 inhibitor drugs used to lower lipid levels.
- 21.2.4 Explain the client education related to statins (HMG-CoA reductase inhibitors) and PCSK9 inhibitor drugs used to lower lipid levels.

Statin drugs are some of the most common drugs taken in the United States and are the mainstays of cholesterol-lowering pharmacologic therapy. Depending on the dose, they can reduce LDL-cholesterol levels by greater than half. Statins are oral drugs that work by inhibiting HMG-CoA reductase, which is an enzyme used in cholesterol synthesis. In addition to their effect on LDL-cholesterol levels, statin medications have additional beneficial effects that are unrelated to their effect on cholesterol; these are called **pleiotropic effects**. Some examples of pleiotropic effects are anti-inflammatory, antioxidant, antiproliferative, and plaque-stabilizing actions, which contribute to their efficacy in preventing and treating CAD (Choudhary et al., 2023). Many different statin medications are available. Much of the information regarding statin medications applies to all drugs in this class; however, there are some differences among the agents. Some of the major differentiators within the statin class of medications are administration instructions, potency, and drug interactions.

Because cholesterol is made in the body at night, it is common for statin medications to be taken at bedtime. This timing allows the highest concentration of the drug to be available when cholesterol synthesis is most active, leading to the greatest therapeutic efficacy. However, drugs with a longer half-life, such as rosuvastatin and atorvastatin, can be taken at any time of day because they remain in the body longer.

Statin medications vary in their potency, or the magnitude of cholesterol lowering that occurs upon administration to a client. The drug/dose combinations are classified by this potency: high intensity (greater than 50%), moderate intensity (30%–49%), and low intensity (less than 30%; Table 21.3). Based on their high potency, atorvastatin and rosuvastatin are some of the most frequently prescribed statin medications.

High Intensity	Moderate Intensity	Low Intensity
Atorvastatin 40–80 mg Rosuvastatin 20–40 mg	Atorvastatin 10–20 mg Rosuvastatin 5–10 mg Simvastatin 20–40 mg Pravastatin 40–80 mg Lovastatin 40–80 mg Fluvastatin XL 80 mg Pitavastatin 1–4 mg	Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg

TABLE 21.3 **Statin Drugs Classified by Intensity of Ability to Lower Cholesterol** (source: Adapted from Grundy et al., 2019)

The drug interaction profile of each statin depends on its metabolic pathway. Simvastatin and lovastatin have a high likelihood of interacting with many other drugs. Their metabolism relies heavily on cytochrome enzymes, and if another drug inhibits their metabolism, the statin concentrations increase, putting the client at risk for adverse events. Pravastatin has relatively fewer drug interactions because it relies less on metabolism via cytochrome enzymes in the liver for metabolism. It is often considered the drug of choice for clients who must take highly interacting drugs, such as certain immunosuppressants after an organ transplant.

Nurses should be familiar with the American Heart Association's recommendations for management of drug interactions with statins (https://openstax.org/r/ahajournalso). The tables provide summaries of selected interactions and their management recommendations (Wiggins et al., 2016). If drug interactions are present, the choice of drug depends on the specific indication for statin therapy and other medications the client must take.

PCSK9 inhibitors are a newer class of drugs that bind to PCSK9 proteins, rendering them unable to function.

Inhibition of PCSK9 leads to less degradation of LDL receptors, making them more available to remove LDL-cholesterol from the circulation. PCSK9 inhibitors are some of the most potent LDL-lowering medications available and can lower LDL-cholesterol by 43%–64% (Grundy et al., 2019). PCSK9 inhibitors are monoclonal antibodies and require ongoing administration by injection. They are generally well tolerated, although long-term safety has not been well established. One of the disadvantages of PCSK9 inhibitors is the cost—roughly $14,000 per year (Grundy et al., 2019; based on list price from mid-2018).

Inclisiran is another drug that targets PCSK9, but it works differently than the PCSK9 inhibitors, and it is not a monoclonal antibody. It prevents the formation of PCSK9 altogether, leading to a therapeutic effect similar to that of the PCSK9 inhibitors. Like the PCSK9 inhibitors, it is given by subcutaneous injection; however, a health care professional should administer it. After an initial 3-month loading phase, it is administered just twice a year. No specific monitoring is required after injection.

Table 21.4 lists common statins and PCSK9 inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Atorvastatin (Lipitor)	10–80 mg orally daily.
Fluvastatin (Lescol XL)	20–80 mg orally daily in 2 divided doses.
Pitavastatin (Livalo)	1–4 mg orally daily.
Pravastatin (Pravachol)	10–80 mg orally daily.
Rosuvastatin (Crestor)	5–40 mg orally daily.
Simvastatin (Zocor)	10–40 mg orally daily at bedtime.
Alirocumab (Praluent)	*Primary hyperlipidemia and heterozygous familial hypercholesterolemia:* 75 mg subcutaneously every 2 weeks or 300 mg subcutaneously every 4 weeks; if inadequate response, may adjust to 150 mg subcutaneously every 2 weeks. *Homozygous familial hypercholesterolemia:* 150 mg subcutaneously every 2 weeks.
Evolocumab (Repatha)	*Primary hyperlipidemia and heterozygous familial hypercholesterolemia:* 140 mg subcutaneously every 2 weeks or 420 mg subcutaneously once monthly. *Homozygous familial hypercholesterolemia:* 420 mg subcutaneously once monthly; can be increased to 420 mg subcutaneously every 2 weeks if a clinically meaningful response is not achieved.
Inclisiran (Leqvio)	*Adjunct to diet and statin therapy for treatment of heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease in clients who require additional lowering of LDL-cholesterol:* 284 mg administered subcutaneously once, and then again at 3 months, and then every 6 months thereafter.

TABLE 21.4 **Drug Emphasis Table: Statins and PCSK9 Inhibitors** (source: https://dailymed.nlm.nih.gov/dailymed/)

Statins

Some of the most popular statin medications are atorvastatin, simvastatin, rosuvastatin, and pravastatin.

Rosuvastatin

Rosuvastatin is the most potent statin medication. At a dosage of 20–40 mg per day, it is one of only two statin medications classified as high intensity and is recommended for individuals with the greatest cardiovascular risk. Unlike some other statins, rosuvastatin may be taken at any time of the day because it has a long half-life of 19 hours. The capsules or tablets should be swallowed whole and not crushed or chewed. Rosuvastatin is metabolized by CYP2C9, so it interacts with other drugs that affect that enzyme. Rosuvastatin is a hydrophilic (water-soluble) statin, which may confer a lower risk of myopathy because it does not easily enter the muscle.

Atorvastatin

Atorvastatin is another potent statin medication. At a dosage of 40–80 mg per day, it is also classified as high intensity and is recommended for individuals with the greatest cardiovascular risk. It may be taken at any time of day because of its long half-life. It is metabolized by CYP3A4, so it interacts with other drugs that affect that enzyme. The metabolizing enzyme for atorvastatin is different from that for rosuvastatin, so the drug interaction profiles vary as well. Atorvastatin is a lipophilic (fat-soluble) statin, which may allow it to penetrate the muscle tissue and lead more readily to myopathy.

Table 21.5 is a drug prototype table for statins featuring atorvastatin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Statin **Mechanism of Action** Inhibits HMG-CoA reductase, an enzyme involved in cholesterol synthesis	**Drug Dosage** 10–80 mg orally once daily.
Indications To reduce the risk of cardiovascular events in specific populations Primary hyperlipidemia Heterozygous and homozygous familial hypercholesterolemia Primary dysbetaliproteinemia Hypertriglyceridemia **Therapeutic Effects** Decreases LDL-cholesterol level Decreases triglyceride level	**Drug Interactions** Rifampin Oral contraceptives Digoxin Amiodarone **Food Interactions** Grapefruit juice
Adverse Effects Myopathy Nasopharyngitis Arthralgia/myalgia Diarrhea Pain in extremities Urinary tract infection	**Contraindications** Acute liver failure or decompensated cirrhosis Hypersensitivity to atorvastatin or other excipients Caution: Myopathy and rhabdomyolysis Immune-mediated necrotizing myopathy Hepatic dysfunction

TABLE 21.5 **Drug Prototype Table: Atorvastatin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Simvastatin

At its highest prescribed doses, simvastatin is considered a moderate-intensity statin. Therefore, it is not appropriate for clients who have very high cardiovascular risk. Nurses should instruct clients to take simvastatin in the evening because of its shorter half-life compared to rosuvastatin or atorvastatin. Simvastatin is metabolized to a great extent by CYP3A4, and drug interactions influence its concentrations in the body. The U.S. Food and Drug Administration (FDA) has issued a warning regarding dose limitations when simvastatin is used concomitantly with amiodarone. (See the FDA website for the most recent update to that warning (https://openstax.org/r/fdagovdrugsd).) It is also a highly lipophilic statin. The high potential for drug interactions, combined with lipophilicity that may facilitate entry into muscle tissue, may confer greater risks for clients taking simvastatin rather than other options.

SAFETY ALERT

Simvastatin

Clients should not take simvastatin 80 mg because the risk of muscle-related adverse events is unacceptably high. More information about restrictions, contraindications, and dose limitations (https://openstax.org/r/fdagovdrugsdr) can be found online.

Pravastatin

Pravastatin is another statin medication. At its highest doses, it is considered a moderate-intensity statin. Thus, it is not considered appropriate for clients who have high cardiovascular risk. Pravastatin has a comparatively lower risk of drug interactions because it is not metabolized as highly by CYP enzymes, although some interactions are still possible. In addition, is hydrophilic; these two aspects may confer a lower risk for myopathy. Pravastatin is often considered a drug of choice in clients who take multiple medications and have an increased risk of drug interactions or those who cannot tolerate other statins due to adverse effects. However, it is not potent enough to be a first-line option for many clients.

PCSK9 Inhibitors

The two PCSK9 inhibitors currently available are alirocumab and evolocumab. The drugs are relatively similar but vary in their dosing (Table 21.4). Both are given as subcutaneous injections that can be self-administered by the client.

Adverse Effects and Contraindications

Some of the most common and limiting adverse effects associated with statins are muscular in nature. Myalgia, or muscle pain, is common and occurred in 5%–10% of clients taking statin therapy in observational studies (Grundy et al., 2019). Myositis is rare and is characterized by muscular pain or weakness and elevated levels of the enzyme creatine kinase, indicating muscle breakdown. Rhabdomyolysis is the most severe muscular side effect of statin therapy. It is characterized by severe muscle breakdown and creatine kinase (CK) levels 10-fold greater than normal. The byproducts of muscle breakdown can cause kidney toxicity, which can be fatal. Some statins have a higher propensity to cause myopathy. This risk may be related to their drug interactions. If clients take a drug that raises the concentration of their statin medication in their blood, they may have a higher risk for adverse effects. The risk of myopathy may also be related to how hydrophilic or lipophilic the drug is. Statins that are more highly lipophilic can more easily enter the muscle and cause toxicity.

Statins are associated with new-onset diabetes, most commonly in clients who have other risk factors for diabetes, such as obesity or metabolic syndrome. Infrequently, statins have been associated with elevations in transaminase. Prior to 2012, liver function was frequently monitored in clients taking statin medications because of concerns for and association with liver failure. However, in 2012 the FDA revised the recommendation (https://openstax.org/r/fdagovdrugsdrugsafe) for monitoring liver function and now recommends that liver enzymes be tested before starting statin therapy and only as clinically indicated thereafter. This change was made because hepatic failure due to statin medications is rare, and monitoring liver enzymes does not detect or prevent serious liver injury.

Previously, statin medications carried a strong warning against use in pregnancy and were considered absolutely contraindicated. In 2021, based on a review of evidence, the FDA downgraded this strong warning to a recommendation. The FDA now recommends that health care providers discontinue statin use in most pregnant clients but that they also should consider the individual client's ongoing therapeutic needs.

The most common adverse effects of PCSK9 inhibitors are injection site reactions, which are usually mild. Hypersensitivity reactions are also possible. PCSK9 inhibitors are contraindicated in clients with a history of hypersensitivity to any drug within the class.

The most common adverse effects of inclisiran are injection site reactions. It has no absolute contraindications.

Nursing Implications

The nurse should do the following for clients taking statin medications:

- Teach clients about nonpharmacologic modalities for cardiovascular risk reduction and lipid lowering.
- Obtain an accurate home medication list and check it for possible drug and food interactions.
- Monitor for signs and symptoms of muscle-related adverse effects.
- Ensure appropriate monitoring of LDL-cholesterol levels.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

The nurse should do the following for clients taking PCSK9 inhibitors:

- Teach clients about nonpharmacologic modalities for cardiovascular risk reduction and lipid lowering.
- Teach clients how to administer their medications.
- Monitor for hypersensitivity reactions and injection site reactions.
- Instruct the client on the technique to self-administer the medication.
- Ensure appropriate monitoring of LDL-cholesterol levels.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

The nurse should do the following for clients taking inclisiran:

- Administer the drug subcutaneously in the abdomen, upper arm, or thigh.
- Avoid injecting into areas of active skin disease or injury.
- Refrain from giving the medication if it is discolored or contains particulate matter.
- Monitor for injection site reactions.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a statin drug should:

- Maintain a heart-healthy diet.
- Engage in activity as directed by their health care provider.
- Take their statin medication in the evening if needed.
- Report any muscular signs and symptoms to their health care provider, including muscle pain, muscle weakness, and very dark urine, which can indicate rhabdomyolysis.
- Report any symptoms of liver failure (rare) to their provider: yellowish skin or eyes, nausea, vomiting, upper right abdominal pain, general feeling of unwellness.

The client taking a PCSK9 inhibitor should:

- Maintain a heart-healthy diet.
- Engage in activity as directed by their health care provider.
- Store the drug in the refrigerator in the original carton and protect it from light and freezing.
- Discard the medication if it is left at room temperature for more than 30 days.
- Allow the drug to warm to room temperature for 30–40 minutes prior to administration if refrigerated.
- Avoid using medication that is cloudy, is discolored, or contains particles.
- Administer into areas of the thigh, abdomen, or upper arm that are not tender, bruised, red, or indurated.
- Rotate injection sites for each dose.
- If administering a large dose, divide it into two injections and give them consecutively at two different sites.

The client taking inclisiran should:

- Make and keep appointments to have the drug administered by a health care professional.

21.3 Bile Acid Sequestrants, Fibrates, and Niacin

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 21.3.1 Identify the characteristics of bile acid sequestrant, fibrates, and niacin drugs used to lower lipid levels.
- 21.3.2 Explain the indications, action, adverse reactions, and interactions of bile acid sequestrant, fibrates, and niacin drugs used to lower lipid levels.
- 21.3.3 Describe nursing implications of bile acid sequestrant, fibrates, and niacin drugs used to lower lipid levels.
- 21.3.4 Explain the client education related to bile acid sequestrant, fibrates, and niacin drugs used to lower lipid levels.

Bile acid sequestrants, fibrates, and niacin vary in their mechanism, therapeutic effect, and side effect profile. Table 21.6 lists common bile acid sequestrants, fibrates, and niacin and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Cholestyramine (Questran)	*Hyperlipidemia:* Initiate at 4 g orally 1–2 times daily; increase gradually to 8–16 g orally in 2 divided doses; maximum dose 24 g/day.
Cholesevelam (Welchol)	*Hyperlipidemia:* 3.75 g/day orally in 1–2 divided doses.
Colestipol (Colestid)	*Hyperlipidemia (tablets):* Initial dose 2 g orally 1–2 times daily; increase by 2 g orally 1–2 times daily at 1–2-month intervals; maintenance dose is 2–16 g orally once daily or in divided doses.
Fenofibrate (Tricor)	*Hypertriglyceridemia:* 48–145 mg orally once daily; maximum dose is 145 mg. *Primary hypercholesterolemia or mixed dyslipidemia:* Initial dose 145 mg once daily.
Gemfibrozil (Lopid)	*Hypertriglyceridemia:* 1200 mg administered orally in 2 divided doses 30 min before the morning and evening meals.
Niacin	*Hyperlipidemia or hypertriglyceridemia (niacin extended-release prescription product):* Initial dose 500 mg orally at bedtime after a low-fat snack; increase by no more than 500 mg in any 4-week period; maintenance dose is 1000–2000 mg once daily at bedtime.

TABLE 21.6 **Drug Emphasis Table: Bile Acid Sequestrants, Fibrates, and Niacin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Bile Acid Sequestrants

Bile acid sequestrants are a class of drugs that lower cholesterol. Bile acids are made from cholesterol and are released from the small intestine to aid in fat digestion after the individual consumes food. The majority of bile acids are reabsorbed back into the body after use. Bile acid sequestrants work by binding to bile acids in the intestine, which reduces their absorption and decreases the amount of bile acids available in the body. The body compensates for this by producing more bile acids from cholesterol, effectively decreasing the amount of cholesterol that remains.

Bile acid sequestrants are often used as second-line therapy for hypercholesterolemia if clients do not achieve sufficient goals using first-line therapy or if they are intolerant to first-line therapy. Bile acid sequestrants can be expected to lower the LDL-cholesterol levels by 15%–30% (Grundy et al., 2019). Response to therapy is monitored by obtaining LDL-cholesterol levels. These drugs are orally administered and are not absorbed into the systemic circulation; therefore, they are best taken with meals so that they will encounter the bile acids upon secretion. However, their use is limited by frequency of dosing, an unfavorable gastrointestinal adverse effect profile, and their propensity for interaction with other drugs, which necessitates coordination of administration. Also, outcomes data in cardiovascular disease are lacking when used in combination with statins, the first-line therapy for hypercholesterolemia and cardiovascular risk reduction.

Three bile acid sequestrants are used for treating hyperlipidemia. The drugs have few distinguishing factors beyond the class effects listed here. Some of the differentiators are the available dosage forms (tablets, powder), administration instructions, and FDA-approved indications. These are summarized in Table 21.7; however, it is

always best to check the specific product labeling for administration instructions.

Drug	FDA-Approved Indications	Available Dosage Forms	Special Administration Instructions
Cholestyramine	• Cholesterol reduction (primary hyperlipidemia) • Slow or reverse progression of coronary atherosclerosis • Pruritus associated with partial biliary obstruction	• Oral powder (bulk with scoop or dose-sized packets)	*Oral powder:* • Should not be taken in dry form. • Mix with water or other fluids before ingesting.
Colesevelam	• Cholesterol reduction (primary hyperlipidemia and pediatric clients aged 10–17 years with heterozygous familial cholesterolemia) • Blood sugar reduction in clients with type 2 diabetes	• Oral powder (dose-sized packets) • Oral tablet	*Oral powder:* • Should not be taken in dry form. • Mix contents of 1 packet with 1 cup of water, fruit juice, or diet soft drink. Stir well and drink.
Colestipol	• Cholesterol reduction (primary hyperlipidemia)	• Oral powder (bulk with scoop or dose-sized packets) • Oral tablets	*Oral powder:* • Should never be taken in dry form. • Mix dose with 3 oz or more of water or other beverages; use pulpy juice to minimize complaints about its consistency. • Stir until mixed and then drink. • Rinse the glass with a small amount of additional beverage to make sure all the medication is taken. • May also be mixed with breakfast cereals, soups with high fluid content, or pulpy fruits such as crushed pineapple, pears, peaches, or fruit cocktail.

TABLE 21.7 **Comparison of Bile Acid Sequestrants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Fibrates

Fibrates are a group of oral drugs that are used primarily to treat hypertriglyceridemia. They include fenofibric acid, fenofibrate, and gemfibrozil. They work by activating peroxisome proliferator-activated receptors. The primary result of this activation is lower triglyceride levels via increased expression of lipoprotein lipase, an enzyme that breaks down triglycerides. Fibrates also lead to increased HDL-cholesterol and mildly lower LDL-cholesterol levels; however, they are not typically recommended for those uses (Grundy et al., 2019). Adverse effects of fibrates include increased serum transaminase, creatine phosphokinase (CPK), and creatinine levels; myopathy; cholelithiasis; and venous thrombosis.

Fenofibric Acid Derivatives

Fenofibric acid is an active drug that directly stimulates peroxisome proliferator-activated receptors as described

above. It is available in the active form under the brand name Fibricor and as generic drugs. An inactive form called fenofibrate is also available; this form converts to fenofibric acid in the body after ingestion. Some of the available dosage forms of fenofibrate are Antara, Lipofen, Fenoglide, Tricor, Trilipix (choline fenofibrate), and their respective generic formulations. The various fenofibrate dosage forms are not bioequivalent and cannot be substituted for each other or for fenofibric acid on a milligram-per-milligram basis; they use different types of medication delivery technology to ensure absorption, including micronized particles, nanocrystals, and different salt forms.

Table 21.8 is a drug prototype table for fenofibric acid derivatives featuring fenofibrate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Fibric acid **Mechanism of Action** Activates peroxisome proliferator-activated receptors to increase breakdown of triglycerides	**Drug Dosage** *Primary hypercholesterolemia or mixed dyslipidemia:* Initial dose 145 mg orally once daily; maximum dose 145 mg once daily. *Severe hypertriglyceridemia:* Initial dose 48–145 mg once daily; maximum dose 145 mg once daily.
Indications Primary hyperlipidemia or mixed dyslipidemia Severe hypertriglyceridemia **Therapeutic Effects** Reduces LDL-cholesterol, total cholesterol, triglycerides, and apolipoprotein B; increases HDL-cholesterol	**Drug Interactions** Warfarin Immunosuppressants Bile acid sequestrants Colchicine Statins **Food Interactions** No significant interactions
Adverse Effects Abnormal liver function tests, including increased aspartate aminotransferase (AST), alanine aminotransferase (ALT), and creatine phosphokinase (CPK) levels Rhinitis	**Contraindications** Severe renal dysfunction, including dialysis Active liver disease Gallbladder disease Hypersensitivity Lactation Caution: Hepatotoxicity Myopathy and rhabdomyolysis Increases in serum creatinine Cholelithiasis

TABLE 21.8 **Drug Prototype Table: Fenofibrate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Gemfibrozil

Gemfibrozil is another fibrate approved for the treatment of hypertriglyceridemia and for primary prevention of CAD in clients who have failed to respond to lifestyle changes and other pharmacologic therapies. Gemfibrozil is generally administered orally, twice daily, 30 minutes before breakfast and dinner. The most common adverse events are dyspepsia, abdominal pain, and diarrhea. Less commonly, abnormal liver function tests and worsening renal function in those with baseline dysfunction have been reported. It is contraindicated in clients with severe hepatic or renal disease, preexisting gallbladder disease, or hypersensitivity to gemfibrozil.

Gemfibrozil is associated with several notable drug interactions. The concomitant use of gemfibrozil and rosuvastatin or simvastatin is contraindicated because of the risk of myopathy and rhabdomyolysis. If the client needs to take both a fibrate and a statin, it is safer to use a fenofibric acid derivative. Similarly, a client taking gemfibrozil with colchicine should be monitored for the same concerns of myopathy and rhabdomyolysis. Concomitant use with warfarin places the client at risk for bleeding, so frequent monitoring of the international normalized ratio is recommended until stabilization.

SAFETY ALERT

Gemfibrozil

The nurse should clarify any medication orders that use abbreviations. For example, gemfibrozil could be abbreviated as "gem." This could be confused with gemcitabine, a chemotherapy agent, with severe consequences. Learn more about error-prone abbreviations (https://openstax.org/r/ismporgresources) like this one by visiting the website for the Institute for Safe Medication Practices.

Niacin

Niacin (vitamin B_3) is a water-soluble vitamin. The chemical name for niacin is nicotinic acid. It is approved for treatment of hyperlipidemia, dyslipidemia, and hypertriglyceridemia; for secondary prevention of myocardial infarction; and, in combination with a bile acid sequestrant, for slowing the progression or promoting the regression of atherosclerotic disease. The specific mechanism of action of niacin in dyslipidemia is not well understood. It may increase the activity of lipoprotein lipase, the main enzyme that is affected by fibrates, or it may increase the rate of removal from plasma and decrease the rate of synthesis of LDL-cholesterol. The therapeutic effect in dyslipidemia is a reduction in triglyceride, LDL-cholesterol, and total cholesterol levels as well as an increase in HDL-cholesterol levels.

Niacin is available in various dosage forms. Many are considered dietary supplements and thus are not regulated by the FDA. Some of these dietary supplements are marketed as "flush-free" niacin; however, these flush-free versions have been shown to contain no free nicotinic acid and should not be used to treat dyslipidemia (National Institutes of Health, 2022). Prescription niacin products include extended-release and immediate-release formulations. Nurses should be aware that the various niacin preparations are not interchangeable on a milligram-per-milligram basis.

Adverse Effects and Contraindications

Bile acid sequestrants. Because these drugs are not absorbed into the systemic circulation, systemic adverse effects are limited; side effects from bile acid sequestrants are generally related to their effect on the gastrointestinal system. Constipation is the most common one; it can be severe and can aggravate hemorrhoids. Clients can minimize constipation by starting doses cautiously, taking one per day. It can also be managed with increased fluids and dietary fiber and, if needed, a stool softener. Other gastrointestinal adverse effects include abdominal pain, heartburn, loss of appetite, indigestion, diarrhea, and upset stomach.

Bile acid sequestrants also can cause an increase in triglyceride levels, which is typically mild. However, in clients with a triglyceride level of 300 mg/dL or higher at baseline, hypertriglyceridemia can be severe. With long-term therapy of high doses, absorption of some fat-soluble nutrients may be decreased, and supplementation of vitamins A, D, E, and K may be needed. In extreme cases, bleeding can occur due to an induced deficiency of vitamin K, which is needed for the synthesis of clotting factors. Additionally, bile acid sequestrants can interfere with the absorption of some drugs. Because of this, it is recommended that clients take other drugs at least 1 hour before or 3–4 hours after taking a bile acid sequestrant (Grundy et al., 2019).

Because of the high incidence of constipation, bile acid sequestrants are contraindicated in clients with a history of bowel obstruction. Because these drugs can increase triglycerides, they also are contraindicated in clients who have baseline hypertriglyceridemia or a history of pancreatitis due to hypertriglyceridemia.

Fibrates. The most common adverse effects of fibrates are elevated liver enzymes, increases in serum creatinine, and myopathy, especially when fibrates are combined with statin medications. They should not be used in clients who have active liver disease, gallbladder disease, severe renal dysfunction, or hypersensitivity (Singh & Correa, 2023).

Niacin. The most limiting adverse effect of niacin is flushing, which is most prominent in the immediate-release preparations. This occurs because niacin increases prostaglandins in capillaries, leading to cutaneous vasodilation. It can be managed by slowing down the niacin absorption rate by using a slower-release (extended-release) version or by administering a nonsteroidal anti-inflammatory drug (NSAID) such as aspirin 30 minutes before niacin

administration (National Institutes of Health, 2022). Clients taking niacin can minimize flushing by avoiding hot drinks and alcoholic beverages. Significant adverse effects include hepatotoxicity, insulin resistance, hyperglycemia, and hyperuricemia (National Institutes of Health, 2022).

Niacin is contraindicated in clients with active liver disease, unexplained or persistent elevations in hepatic transaminase levels, active peptic ulcer disease, arterial bleeding, or hypersensitivity to niacin or components of the formulation.

Nursing Implications

The nurse should do the following for clients taking bile acid sequestrants:

- Monitor for constipation and instruct client about appropriate management (increase fluids and dietary fiber and, if needed, take a stool softener).
- Administer other drugs at least 1 hour before or 3–4 hours after bile acid sequestrant administration.
- Mix powder dosage forms with fluid as appropriate.
- Monitor for deficiency of fat-soluble nutrients and recommend supplementation when needed.
- Administer with meals as directed by the health care provider.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

The nurse should do the following for clients taking fibrates:

- Obtain an accurate home medication list to assess for drug interactions.
- Avoid direct substitution of different forms of fenofibric acid because they are not interchangeable.
- Monitor for signs and symptoms of muscle-related adverse effects, especially when coadministered with a statin.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

The nurse should do the following for clients taking niacin:

- Assist the client in choosing appropriate over-the-counter versions when needed. Avoid flush-free niacin and choose extended-release products to maximize efficacy and minimize flushing.
- Administer an NSAID prior to administration if directed by the health care provider; if the client is already taking low-dose aspirin, the aspirin dose can be administered before niacin to limit additional NSAIDs.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a bile acid sequestrant should:

- Take other drugs at least 1 hour before or 3–4 hours after bile acid sequestrant administration.
- Alert their health care provider, increase fluids and dietary fiber, and, if needed, take a stool softener if they experience constipation.
- Administer with meals as directed by their health care provider.
- Take vitamin supplementation if instructed to do so by their health care provider.

The client taking a fibrate should:

- Keep an accurate medication list so that health care professionals can assess for drug interactions.
- Monitor for adverse events and alert their health care provider with any concerns.

The client taking niacin should:

- Avoid choosing flush-free niacin for managing lipid levels.
- Ask their health care provider about possibly taking an NSAID before their niacin drug.
- Avoid hot drinks and alcoholic beverages around the time of administration to minimize flushing.

21.4 Cholesterol Absorption Inhibitors

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 21.4.1 Identify the characteristics of cholesterol absorption inhibitor drugs used to lower lipid levels.
- 21.4.2 Explain the indications, action, adverse reactions, and interactions of cholesterol absorption inhibitor drugs used to lower lipid levels.
- 21.4.3 Describe nursing implications of cholesterol absorption inhibitor drugs used to lower lipid levels.
- 21.4.4 Explain the client education related to cholesterol absorption inhibitor drugs used to lower lipid levels.

Ezetimibe is a cholesterol absorption inhibitor. It works by inhibiting the cholesterol transporter called Niemann-Pick C1-Like 1 (NPC1L1). It lowers LDL-cholesterol levels by 13%–20% (Grundy et al., 2019).

Cholesterol Absorption Inhibitor: Ezetimibe

One cholesterol absorption inhibitor will be discussed: ezetimibe. Table 21.9 is a drug prototype table for cholesterol absorption inhibitors featuring ezetimibe. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Cholesterol absorption inhibitor **Mechanism of Action** Inhibits the Niemann-Pick C1-Like 1 cholesterol transporter, which is responsible for absorption of cholesterol in the small intestine	**Drug Dosage** 10 mg orally once daily.
Indications Primary hypercholesterolemia Homozygous familial hypercholesterolemia Homozygous sitosterolemia **Therapeutic Effects** Lowers LDL-cholesterol levels	**Drug Interactions** Cyclosporine Fenofibrate/fibrates Cholestyramine **Food Interactions** No significant interactions
Adverse Effects Upper respiratory tract infection Diarrhea Arthralgia Sinusitis Pain in extremities Angioedema	**Contraindications** Active liver disease, including unexplained persistent elevations in hepatic transaminase levels Pregnancy or possible pregnancy Lactation Known hypersensitivity to product components Caution: Not recommended in clients with moderate or severe hepatic impairment Monitor liver enzyme levels when taken with a statin Skeletal muscle effects (e.g., myopathy and rhabdomyolysis) have been reported

TABLE 21.9 **Drug Prototype Table: Ezetimibe** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Ezetimibe

Ezetimibe is available as a single-drug tablet with the brand name Zetia. It is also one of the drugs included in the combination product sold under the brand name Vytorin, which contains both ezetimibe and simvastatin. Nurses

should be careful to avoid confusing the single drug and the combination products.

Adverse Effects and Contraindications

The most significant adverse events associated with ezetimibe are liver enzyme abnormalities, myopathy, and rhabdomyolysis, especially when the drug is combined with statin medications. Another adverse effect is diarrhea.

Ezetimibe should not be used in clients with active liver disease or unexplained elevations in transaminase levels, those who are pregnant or breastfeeding, or those with hypersensitivity to the drug or any of its product components.

Nursing Implications

The nurse should do the following for clients taking ezetimibe:

- Monitor hepatic transaminase levels (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]).
- Monitor for adverse events such as liver toxicity and diarrhea.
- Monitor for muscle-related adverse events, especially when the drug is used in combination with statins.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking ezetimibe should:

- Take the medication daily, taking no more than one dose per day.
- Refrain from taking the medication when pregnant.
- Notify their health care provider about any muscle pain or weakness.
- Report any adverse events to their health care provider.

Chapter Summary

This chapter reviewed lipid-lowering drugs. It introduced lipoproteins, including their metabolism and their connection to CAD. Many classes of lipid-lowering medications were described, along with salient nursing implications and client education.

Key Terms

atherosclerosis formation of fatty material called plaques on inner arterial walls

cholesterol major sterol in the body; important for the structure of cell membranes and the production of hormones, bile acids, and vitamin D

chylomicrons lipoproteins produced by enterocytes in the gut; carry triglycerides to the tissues after dietary consumption

dyslipidemia abnormal lipid levels or an imbalance of lipids in the blood

familial hypercholesterolemia genetic disorder that manifests as very high cholesterol levels that can cause early cardiovascular disease

high-density lipoproteins (HDL or HDL-cholesterol) cholesterol-rich lipoproteins made by the liver that function to remove cholesterol from the circulation; "good cholesterol"

HMG CoA reductase enzyme involved in cholesterol biosynthesis

hypercholesterolemia excessive blood levels of cholesterol

hyperlipidemia excessive blood levels of lipids

hypertriglyceridemia excessive blood levels of triglycerides

lipoprotein lipase enzyme that breaks down triglycerides into free fatty acids

lipoproteins combinations of lipids and proteins that carry cholesterol and triglycerides in the blood

low-density lipoproteins (LDL or LDL-cholesterol) cholesterol-rich lipoprotein made by the liver and implicated in the development of atherosclerosis; "bad cholesterol"

pleiotropic effects additional beneficial effects of statin medications unrelated to their lipid-lowering effects

triglycerides main dietary source of fat; composed of three long fatty acid chains attached to a glycerol backbone

very low-density lipoproteins (VLDL) triglyceride-rich lipoprotein made by the liver

Review Questions

1. A nurse is explaining a client's lipid panel results. Which statement by the client indicates a need for further teaching?
   a. "LDL-cholesterol is 'bad cholesterol.'"
   b. "Medications can be used to increase my triglyceride levels."
   c. "HDL-cholesterol is 'good cholesterol.'"
   d. "Medications can decrease my cholesterol levels."

2. A nurse is explaining administration instructions for a client who is starting alirocumab, a PCSK9 inhibitor. Which statement will the nurse include in the instructions?
   a. It can be taken orally at bedtime.
   b. It is self-administered as a subcutaneous injection by the client.
   c. It is administered as a subcutaneous injection by a health care professional.
   d. It comes in a powder form that must be mixed with liquid before taking.

3. A client began treatment for severe hypertriglyceridemia and goes to the clinic for follow-up. Which medication does the nurse expect to find on the client's home medication list?
   a. Ezetimibe
   b. Cholestyramine
   c. Colesevelam
   d. Fenofibrate

4. A client calls the nurse because they experienced intolerable flushing after taking over-the-counter niacin. Which intervention might the nurse recommend?
   a. Take flush-free niacin.

b. Switch to immediate-release niacin.
c. Take aspirin 30 minutes before taking niacin.
d. Take niacin with an alcoholic beverage.

5. A nurse is evaluating a follow-up lipid panel in a client who recently began taking ezetimibe. Which of the following changes would the nurse expect to see?
a. Decreased HDL-cholesterol level
b. Decreased LDL-cholesterol level
c. Increased triglyceride level
d. Increased VLDL level

6. A nurse educator is training new nurses on the cardiac step-down unit about medications administered on the unit. Which statement indicates understanding of the drug cholestyramine?
a. It can cause diarrhea as the major adverse effect.
b. It should be taken in the morning when cholesterol synthesis is highest.
c. It is available as an oral powder that must be mixed with fluid before taking.
d. It works primarily to lower triglyceride levels in clients with hypertriglyceridemia.

7. A client is admitted to the cardiac unit after undergoing stent placement after an acute myocardial infarction. The provider states that the client will need high-intensity statin therapy. Which medication does the nurse expect to be ordered for the client?
a. Simvastatin
b. Pravastatin
c. Rosuvastatin
d. Fluvastatin

8. Which of the following statements is true about pravastatin?
a. It is considered a hydrophilic statin, which means it may confer a lower risk of myalgia compared with other statins.
b. The FDA has issued a statement that doses of 80 mg are no longer appropriate due to myalgia risk.
c. It is metabolized by CYP3A4 and is subject to many drug interactions.
d. It is considered a high-intensity statin.

9. A client with a past medical history of CAD has been taking rosuvastatin 40 mg orally daily for 1 month and has a follow-up LDL-cholesterol level of 135 mg/dL, which exceeds their goal LDL-cholesterol level of 70 mg/dL. Which would be an appropriate next step for the client?
a. Add gemfibrozil for combination therapy.
b. Change administration to bedtime rather than morning.
c. Change to pravastatin 80 mg orally daily.
d. Add ezetimibe for combination therapy.

10. A client is taking atorvastatin. Which severe adverse drug reaction should the client be monitored for?
a. Rhabdomyolysis
b. Stroke
c. Severe constipation
d. Myocardial infarction

CHAPTER 22
Cardiac Emergency and Shock Drugs

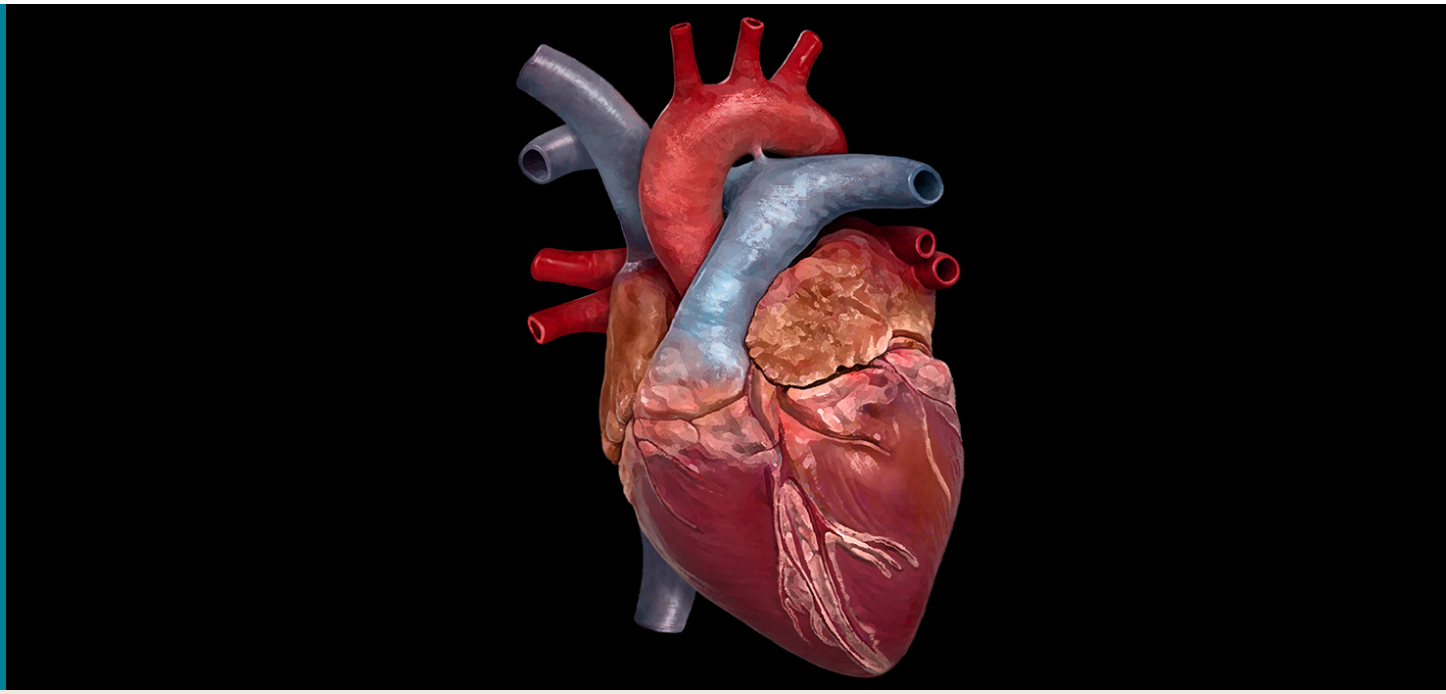


FIGURE 22.1 The heart is the primary organ of the cardiovascular system, controlling circulation and blood flow for the entire body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Cardiac emergencies are life-threatening events that can include acute myocardial infarction, unstable angina, and acute dysrhythmias (abnormal heart rhythms). Acute myocardial infarction and unstable angina occur when the blood supply to the heart is threatened by occlusion of a coronary artery. Both of these processes of cardiac tissue ischemia deprive the tissue of oxygen; in infarction, cell death has occurred in the tissue as a result of this sudden insufficient blood supply. Ischemia and infarction can acutely and significantly affect the heart's ability to pump blood. Dysrhythmias occur when the cardiac conduction system is not functioning correctly and so does not stimulate the heart to contract correctly. Both coronary artery occlusions and acute dysrhythmias can lead to shock, which occurs when tissue perfusion is decreased so much that tissues become ischemic. If shock is not reversed quickly, tissue damage will occur, and eventually cell, tissue, and system death will occur.

22.1 Introduction to Cardiac Emergencies and Shock

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 22.1.1 Describe cardiac emergencies requiring emergency drugs.
- 22.1.2 Describe shock and general treatment guidelines.

Cardiac Emergencies

The primary responsibility of the heart is to generate **cardiac output**. Cardiac output (CO) is a function of heart rate (HR) and stroke volume (SV): $\mathrm{CO} = \mathrm{HR} \times \mathrm{SV}$. Normal resting cardiac output is 4–5 L/min. Heart rate is the

number of times the heart beats per minute. Stroke volume is the amount of blood pumped out of the left ventricle with each heartbeat. In order for the heart to maintain cardiac output, both the electrical system of the heart and the pumping system of the heart must function properly. When the heart pumps blood into the aorta, the first organ that receives blood is the heart itself; coronary arteries branch off the aorta to supply the heart with oxygen and nutrients. The left main coronary artery and the right coronary artery (Figure 22.2) are large arteries that branch into smaller arteries and arterioles to supply the heart. If any type of occlusion exists, then the blood flow to the heart tissue is reduced (**ischemia**), and anoxia and **infarction** may occur.

There are two main types of cells in the heart: cardiac myocytes, which are contractile cells, and cardiac conduction cells, which generate and conduct electrical impulses. If cardiac myocytes are damaged, then the pumping ability of the heart is decreased. If cardiac myocytes die, an **acute myocardial infarction** (commonly referred to as a heart attack) occurs. If cardiac conduction cells die, the conduction system does not function properly, which can affect cardiac output. The cardiac conduction system also depends on appropriate electrolyte plasma levels in order to function optimally.

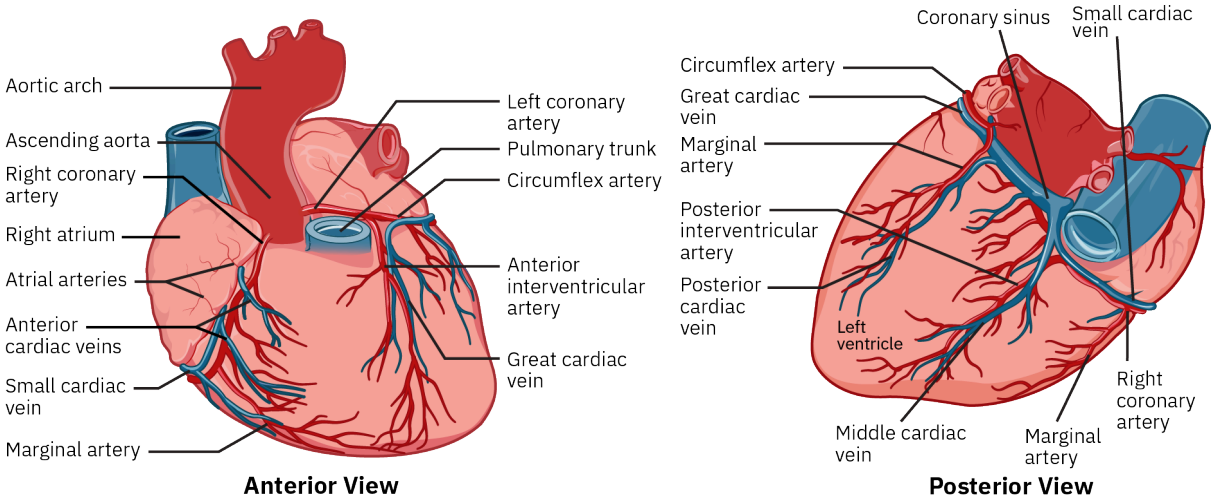


FIGURE 22.2 Both views of the heart show the prominent coronary arteries and surface vessels. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Acute Myocardial Infarction

The heart, just like every other organ in the body, needs oxygen and nutrients to survive. Cardiac tissue receives oxygenated blood from coronary arteries, which branch off from the aorta (Figure 22.2). However, the coronary arteries may become occluded due to various causes, with atherosclerosis, atherosclerotic plaque rupture, and emboli being the most common. If coronary artery occlusion occurs, then oxygenated blood does not reach all of the cardiac tissue. The affected tissue then becomes ischemic, and eventually an acute myocardial infarction (AMI) will occur. It is possible to avert tissue death with timely drugs and procedures.

Figure 22.3 shows an occlusion in the circumflex artery and the common trunk of the left coronary artery. Occlusion in the circumflex artery can lead to ischemia and possible infarction in the apex of the heart.

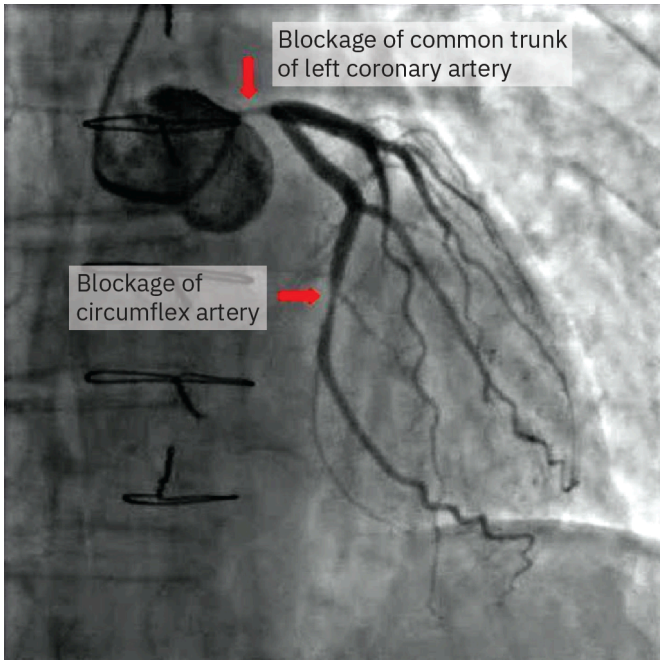


FIGURE 22.3 This coronary angiogram (a type of x-ray) shows a stenosis (blockage) in two different arteries. (credit: modification of work by Pantaleo, M.A., Mandrioli, A., Saponara, M. et al. "Development of coronary artery stenosis in a patient with metastatic renal cell carcinoma treated with sorafenib." BMC Cancer 12, 231 [2012]. https://doi.org/10.1186/1471-2407-12-231; CC BY 2.0)

LINK TO LEARNING

Videos on Coronary Artery Disease

The following videos provide helpful information on atherosclerosis, coronary artery disease, and the pathophysiology of AMI.

Atherosclerosis

Access multimedia content (https://openstax.org/books/pharmacology/pages/22-1-introduction-to-cardiac-emergencies-and-shock)
Coronary artery disease

Access multimedia content (https://openstax.org/books/pharmacology/pages/22-1-introduction-to-cardiac-emergencies-and-shock)
Myocardial infarction pathophysiology

Access multimedia content (https://openstax.org/books/pharmacology/pages/22-1-introduction-to-cardiac-emergencies-and-shock)

Unstable Angina

Angina is the medical term for chest pain caused by cardiac ischemia. Angina occurs when the heart is not getting enough blood flow. There are two types of angina: stable and unstable. Stable angina (discussed in Antihypertensive and Antianginal Drugs) occurs when the heart needs more oxygen but the supply of oxygen is restricted. Once the heart does not need increased oxygen, the angina subsides. Stable angina occurs during exercise or exertion and improves with rest because the cardiac myocytes no longer require an increased oxygen supply. Many people live with stable angina, and medications are available to treat it.

Unstable angina occurs when the heart does not get enough blood flow. Often, the heart does not have an increased demand for oxygen; rather, the supply of oxygen has been decreased most often due to an occlusion of a coronary artery. Because oxygen supply is decreased, the angina will not be relieved with rest. Unstable angina is a medical emergency.

Dysrhythmias

It is important to understand cardiac conduction in order to understand **dysrhythmias**. The heart is truly amazing in that it has the ability to generate electrical impulses. The sinoatrial (SA) node generates impulses that travel through the conduction tissue and stimulate the myocytes to contract. Each impulse leaves the SA node and travels to the atrioventricular (AV) node (during this time, the atria are stimulated to contract), has a brief pause, and then travels down the bundle branches and Purkinje fibers to stimulate ventricular contraction (Figure 22.4).

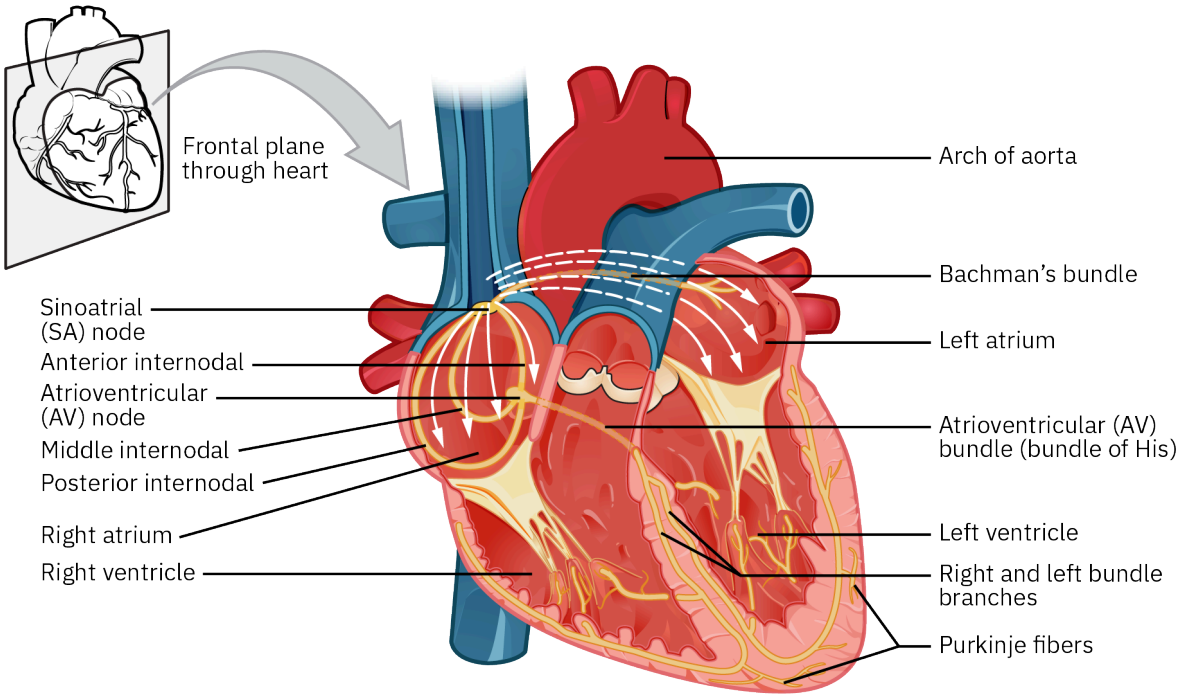


FIGURE 22.4 The SA node generates impulses that travel to the AV node, pause briefly, and then travel down the bundle branches and Purkinje fibers to stimulate ventricular contraction. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The generation and conduction of electrical impulses rely heavily on various electrolytes: potassium, sodium, and calcium. Disturbances in the balance of these electrolytes can lead to serious dysrhythmias. Dysrhythmias can also occur when the conduction system has an interruption in blood supply. The conducting cells of the heart need oxygen and nutrients just as every other cell in the body does. If they do not receive oxygen, they will become ischemic and eventually die. If cells in the conduction pathway die, then that area does not conduct the electrical impulses.

Diagnostics

Unstable Angina and Acute Myocardial Infarction

When an individual is experiencing acute unstable angina or an AMI, the health care provider will first perform a rapid physical assessment based on signs and symptoms and then order specific diagnostics. These may include an electrocardiogram (ECG/EKG), continuous cardiac monitoring, cardiac troponin levels, a complete blood count, a lipid profile, and a basic metabolic profile. Other more advanced diagnostic testing may be performed based on assessment findings. The individual will often undergo cardiac angiography for diagnostics and treatment.

Dysrhythmias

If cardiac dysrhythmia is suspected, the health care provider will perform a rapid physical assessment and order an ECG, which shows changes in heart rhythm and is diagnostic for dysrhythmias. Additional diagnostic tests include a basic metabolic profile to assess potassium, sodium, and calcium levels.

Clinical Manifestations

Clinical manifestations of both unstable angina and AMI include chest pain that may radiate down the left arm or up

to the neck, jaw pain, back pain, shortness of breath, diaphoresis (excessive sweating), nausea and vomiting, anxiety, and a feeling of impending doom. Nurses must be aware that signs and symptoms of AMI vary quite a lot, and some individuals may not feel chest pain at all. Furthermore, female clients often experience symptoms that are more vague or subtle than the ones reported by male clients.

SPECIAL CONSIDERATIONS

Signs and Symptoms of Acute Myocardial Infarction

Many different signs and symptoms can be suggestive of an AMI. Clients will often downplay them and suggest they may be attributed to other causes.

Female clients often experience different signs and symptoms than male clients do during an AMI, such as upper back pressure or lightheadedness. See the American Heart Association website (https://openstax.org/r/topics) for more information on these symptoms.

Clinical manifestations of dysrhythmias include heart palpitations, racing heart rate, chest pain, shortness of breath, anxiety, fatigue, lightheadedness, dizziness, diaphoresis, and syncope (fainting). Life-threatening dysrhythmias often cause syncope to occur rapidly because cardiac output and blood pressure are not maintained.

Nonpharmacologic Treatment

Unstable Angina and Acute Myocardial Infarction

Nonpharmacologic treatment for both unstable angina and AMI includes stopping the activity that caused the pain, having the individual rest, and transporting them by ambulance to the nearest emergency department as soon as possible. They should undergo rapid emergency assessment and, if needed, should be transported to the cardiac catheterization laboratory for coronary artery catheterization, which will provide further diagnostic information and can be used for stent placement in blocked arteries.

Dysrhythmias

If an individual is experiencing a life-threatening dysrhythmia, they should be transported to the nearest emergency department by ambulance. Depending on the type of dysrhythmia, **defibrillation** (administration of electrical shock) may be used to attempt to convert the life-threatening dysrhythmia to normal sinus rhythm (rhythm originating from the SA node).

Shock

All cells in the body require oxygen to make adenosine triphosphate (ATP), which is the primary source of energy that cells use. This process is called aerobic metabolism. Most cells in the body can produce a limited amount of ATP anaerobically (without oxygen), but if oxygen is not eventually present, the cells cannot produce enough ATP to continue functioning, and they will die.

Shock is caused by decreased tissue perfusion that occurs when cells, tissues, and organs do not receive adequate oxygenated blood. Tissues are perfused via the blood pressure (BP), which is a function of cardiac output (CO) and **systemic vascular resistance** (SVR): $\mathrm{BP} = \mathrm{CO} \times \mathrm{SVR}$. Recall that cardiac output is a function of heart rate and stroke volume ($\mathrm{CO} = \mathrm{HR} \times \mathrm{SV}$). Systemic vascular resistance is the amount of resistance in the blood vessels; in other words, it is the pressure that the arterial wall exerts against the circulating blood volume. Systemic vascular resistance is affected by blood vessel diameter, blood vessel length, and fluid viscosity (thickness). Of these three components, blood vessel diameter is by far the most important. A small change in blood vessel diameter can cause a major difference in vascular resistance and overall blood pressure.

Shock is typically classified into four types:

- *Distributive shock* occurs when the normally circulating volume of fluid shifts from intravascular (within the blood vessels) to extravascular (outside of the blood vessels or in the area of the tissues). Because blood pressure depends on systemic vascular resistance, if there is a decreased fluid volume within the vasculature, then there is decreased resistance, and blood pressure is lower. An example of this type of shock is anaphylactic shock.
- *Hypovolemic shock* occurs when there is blood loss. If the bleeding is profound, then the volume in the

vasculature will be reduced, leading to decreased systemic vascular resistance and decreased blood pressure. An example of this is acute blood loss due to a major trauma.

- *Cardiogenic shock* occurs when the heart has been damaged in some way and can no longer maintain adequate cardiac output. When cardiac output decreases, blood pressure decreases in turn. An example of cardiogenic shock is the aftereffect of an AMI. If tissue in the left ventricle dies, then the heart is not able to generate enough force to pump blood, and cardiac output is decreased.
- *Obstructive shock* occurs when some type of blockage in the thoracic cavity (rib cage) impedes the heart's ability to pump. An example of this is cardiac tamponade (increased fluid in the pericardial sac that protects the heart). If there is too much fluid, then the ventricles cannot open enough to allow blood in for filling and therefore cannot pump blood out. Cardiac output is needed to maintain blood pressure, so this reduction in cardiac output will cause a decrease in blood pressure.

This chapter will focus on anaphylactic shock (a type of distributive shock), hypovolemic shock, and cardiogenic shock.

Anaphylactic Shock

Anaphylaxis occurs when the immune system has an overwhelming response to a foreign substance that is not usually harmful to most people. Examples of this type of substance include food and insect stings. In a typical allergic response, the immune system releases inflammatory mediators that cause local vasodilation, but in anaphylaxis, the immune system releases inflammatory mediators throughout the entire body. This response causes systemic vasodilation along with other signs of allergy (rash, pruritis) and bronchoconstriction, which allows plasma to leak from the blood vessels into the tissues. Because systemic vascular resistance is a major component of blood pressure, systemic vasodilation causes hypotension. In anaphylaxis, the resulting profound hypotension is referred to as anaphylactic shock.

Anaphylactic shock can rapidly become life-threatening because the systemic release of inflammatory mediators also affects the respiratory system. In the lungs, the extreme vasodilation causes plasma to leak from blood vessels directly into lung tissue. This is referred to as **pulmonary edema**. The inflammatory mediators also cause smooth muscle constriction. Because the bronchioles are surrounded by smooth muscle, the airways narrow, and breathing is severely restricted. Air flow can become completely cut off and lead to death.

Hypovolemic Shock

Hypovolemic shock results when not enough blood is circulating through the blood vessels. Causes of hypovolemic shock include blood loss due to external or internal bleeding, fluid loss from third-degree burns, and excessive vomiting or diarrhea. For blood pressure to be maintained, an adequate amount of fluid must be present within the blood vessels. If the blood volume is too low, then there will not be enough pressure to maintain systemic vascular resistance, which will cause blood pressure to decrease and the body's tissues to become ischemic. Hypovolemic shock can rapidly become a life-threatening emergency if it is not reversed in a timely fashion.

Cardiogenic Shock

Cardiogenic shock occurs when there has been damage to the cardiac muscle or when an area of cardiac muscle is dead. As already stated, cardiac output is a function of heart rate and stroke volume. Stroke volume is determined by preload, afterload, and contractility. Preload is the amount of blood that returns to the heart (venous return), afterload is the resistance that the heart must pump against, and contractility is the force of the cardiac contraction. In AMI, ventricular muscle cells have died and are no longer able to contract. In ischemia, the decreased blood flow means that cardiac muscle cells do not receive enough oxygen and cannot contract well. Regardless of the precipitating event, contractility is decreased, which negatively affects cardiac output. If cardiac output is decreased, then blood pressure will be decreased, and tissue perfusion will in turn be further decreased.

Diagnostics

Low blood pressure accompanied by clinical signs such as cool, clammy skin; an elevated heart rate; elevated respiratory rate; change in mental status; or reduced level of consciousness are indicative of shock. Because shock is a life-threatening event, if it is suspected, treatment will begin as soon as possible and often before the problem is even definitively diagnosed.

Diagnostics may include an ECG, continuous cardiac monitoring, x-rays, complete blood count, comprehensive

metabolic profile, serum lactate level, blood type and screen testing for possible blood transfusion, and different types of blood cultures (because the cause of the shock may not yet be known).

Clinical Manifestations

Clinical manifestations of shock may include hypotension, tachycardia (heart rate greater than 100 beats/min), tachypnea (fast respiratory rate), cold or clammy skin, decreased mental status, and loss of consciousness. The signs and symptoms can vary depending on the type of shock. In anaphylactic shock, the individual may also have wheezing, stridor, or complete inability to breathe.

22.2 Cardiac Emergency Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 22.2.1 Identify the characteristics of drugs used to treat cardiac emergencies.
- 22.2.2 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat cardiac emergencies.
- 22.2.3 Describe nursing implications of drugs used to treat cardiac emergencies.
- 22.2.4 Explain the client education related to drugs used to treat cardiac emergencies.

The goal of treatment for a client with AMI or unstable angina is restoring the blood supply to the affected area of the heart muscle. Drugs can help either supply more oxygen to the heart (temporarily) or reduce the heart's demand for oxygen. If there is stenosis (narrowing) in a coronary artery, the definitive treatment is having the client undergo stent placement or, if stenting is not an option, coronary artery bypass grafting. It is very important that this treatment not be delayed because it can save heart tissue. Thrombolytic therapy may also be used to dissolve an occlusive clot that is causing the coronary ischemia or infarction. Thrombolytic therapy is discussed in Anticoagulant, Antiplatelet, and Thrombolytic Drugs.

Acute Myocardial Infarction and Unstable Angina Drugs

Four classifications of drugs may be used in emergency situations for AMI and unstable angina: aspirin, oxygen, nitroglycerin, and, occasionally, morphine. In either AMI or unstable angina, the most important thing to consider is blood supply to the heart. If the cardiac cells are not receiving blood, they will become ischemic and eventually will die. Each of the medications is used to enhance oxygen-rich blood flow to the heart.

Aspirin

Salicylic acid (aspirin) has been used for mild pain relief for more than 100 years. (Pain Response Drugs discusses aspirin as a nonopioid analgesic.) It was also found to work as an antiplatelet drug; therefore, it is useful in suspected AMI and unstable angina. Aspirin irreversibly binds to receptors on platelets, which prevents them from sticking to other platelets. Because platelet aggregation is the first step in blood clotting, if this can be reduced, then the heart may receive more blood.

Adverse Effects and Contraindications

Aspirin can cause gastritis and bleeding in the stomach, other parts of the gastrointestinal tract, brain, and spinal cord.

Contraindications to aspirin are allergy to nonsteroidal anti-inflammatory drugs (NSAIDs), asthma, hemophilia, and other blood clotting disorders. Pediatric clients who have suspected viral illnesses should not take aspirin because Reye's syndrome, a potentially fatal complication, could develop. As a precaution, aspirin is generally not used in pediatric clients.

Table 22.1 is a drug prototype table for aspirin used in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Salicylic acid **Mechanism of Action** Irreversibly binds with receptors on platelets, which makes them unable to bind with other platelets	**Drug Dosage** *For acute myocardial infarction or unstable angina:* 325 mg orally (chewed) once. (If client is unable to take orally, administer rectal suppository form.)
Indications Mild pain Platelet inhibition in suspected AMI or unstable angina **Therapeutic Effects** Platelet inhibition Relief of mild pain	**Drug Interactions** Anticoagulants **Food Interactions** Alcohol Tobacco
Adverse Effects Gastrointestinal upset/gastritis Gastrointestinal bleeding	**Contraindications** Allergy to NSAIDs Asthma Hemophilia Pediatric clients (risk of developing Reye's syndrome)

TABLE 22.1 **Drug Prototype Table: Aspirin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking aspirin:

- Assess the client's allergies and verify that they are not allergic to any of the NSAIDs.
- Assess for signs and symptoms of bleeding.
- In the event of suspected AMI or unstable angina, direct the client to chew the aspirin and then swallow it.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking aspirin in an emergency situation should:

- Inform the health care team if they have an allergy to aspirin or other NSAIDs or have a diagnosis of asthma.
- Chew the aspirin tablet before swallowing.

See Anticoagulant, Antiplatelet, and Thrombolytic Drugs for full client teaching guidelines on the use of aspirin in nonemergency situations.

FDA BLACK BOX WARNING

Aspirin

The risk of serious bleeding in the stomach, gastrointestinal tract, brain, and spinal cord is increased with aspirin and other NSAIDs.

Concomitant use of aspirin greater than 100 mg per day can reduce the efficacy of ticagrelor (an antiplatelet medication) and should be avoided.

Oxygen

In an AMI or unstable angina, the cardiac cells are deprived of oxygen. When cells are deprived of oxygen, they eventually will die. Supplemental oxygen may be used if the client's **oxygen saturation** is less than 94% on room air. In the past, oxygen was used immediately for clients with suspected AMI or unstable angina; however, it was not found to be beneficial if used in clients who were already maintaining an oxygen saturation of 95% or more

(Hofmann et al., 2017). Oxygen is typically delivered via nasal cannula starting at 2 L/min and can be titrated to 6 L/min. If the client requires a higher dose to maintain oxygen saturation greater than 94%, then other methods of oxygen delivery should be used.

Nitroglycerin

Nitroglycerin is a **nitrate** and a first-line treatment for clients with AMI or unstable angina. Nitroglycerin is converted to nitrous oxide, which ultimately causes smooth muscles around arteries to relax. Smooth muscle relaxation causes vasodilation. In AMI or unstable angina, the cardiac myocytes are not receiving enough oxygen, and vasodilation allows more oxygen to be delivered to hypoxic cells. In emergency situations, nitroglycerin is administered either sublingually or intravenously.

Antihypertensive and Antianginal Drugs discusses nitrates more extensively.

Adverse Effects and Contraindications

Adverse effects include orthostatic hypotension, tachycardia, paradoxical bradycardia, flushing, peripheral edema, nausea and vomiting, headache, and blurred vision.

Contraindications include allergies to nitrates, concomitant use of phosphodiesterase (PDE) inhibitors such as tadalafil and sildenafil, history of right ventricular infarction, and hypertrophic cardiomyopathy.

Nitrates should be used cautiously in clients who are on chronic diuretic therapy, have low systolic blood pressure, have autonomic nervous system dysregulation, or are pregnant or breastfeeding.

SAFETY ALERT

Nitroglycerin

Nitrates can cause hypotension. In an emergency situation, make sure the client is sitting or lying down before administering nitroglycerin.

Table 22.2 is a drug prototype table for nitroglycerin use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nitrate **Mechanism of Action** Converts to nitric oxide, which ultimately causes smooth muscle relaxation and vasodilation	**Drug Dosage** *For acute myocardial infarction or unstable angina:* *Sublingual:* 0.15–0.6 mg as needed for chest pain every 5 min up to 3 times. *Intravenous (IV):* 5–10 mcg/min up to 100 mcg/min.
Indications For acute relief of pain in suspected acute myocardial infarction or unstable angina **Therapeutic Effects** Relieves pain Increases delivery of oxygen to cardiac tissue	**Drug Interactions** Avanafil Riociguat Sildenafil Tadalafil Vardenafil **Food Interactions** Alcohol Tobacco
Adverse Effects Orthostatic hypotension Tachycardia Paradoxical bradycardia Flushing Peripheral edema Nausea and vomiting Headache Blurred vision	**Contraindications** Allergy to nitrates Hypersensitivity Increased intracranial pressure Cardiomyopathy History of right ventricular infarction Shock Caution: Chronic diuretic therapy Low systolic blood pressure Autonomic system dysregulation Pregnancy Lactation

TABLE 22.2 **Drug Prototype Table: Nitroglycerin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

Refer to Antihypertensive and Antianginal Drugs for a full list of nursing implications for clients prescribed nitrates. In the event of suspected AMI or unstable angina, the health care provider may order sublingual nitroglycerin until an IV line is in place. If the client is receiving IV nitroglycerin, the nurse will receive orders to titrate the nitroglycerin based on pain level and blood pressure.

The nurse should do the following for clients who are receiving nitroglycerin intravenously for chest pain:

- Place the client on continuous cardiac monitoring.
- Monitor vital signs frequently, particularly blood pressure, because nitroglycerin can cause significant hypotension.
- If symptomatic hypotension occurs, do not give the nitroglycerin and inform the health care provider.
- Frequently assess pain level.
- Assess for headache and give pain medication for it as ordered.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving nitroglycerin for unstable angina or AMI should:

- Alert the nurse if any of these occur:
  - Their chest pain changes (either improves or worsens)

- They feel faint
- They experience nausea or vomiting

See Antihypertensive and Antianginal Drugs for full client teaching guidelines on nitroglycerin, including client home usage.

Morphine

Morphine is a potent, fast-acting **opioid agonist**. It binds to opioid receptors in the central and peripheral nervous systems to modulate (decrease) the pain response. Morphine also can help relieve anxiety, which may lower heart rate and reduce the heart's demand for oxygen. For many years, morphine was a first-line drug in the emergency management of AMI and unstable angina, but now it is used if nitroglycerin cannot control the chest pain (Hermiz & Sedhai, 2023). Pain Response Drugs covers opioid agonists in depth.

Adverse Effects and Contraindications

Opioids must be managed carefully due to their potential adverse effects, which include respiratory depression, respiratory arrest, apnea, circulatory depression, shock, cardiac arrest, sedation, lightheadedness, dizziness, nausea, vomiting, and constipation.

Opioids should not be used if the client has a known hypersensitivity to morphine, respiratory depression, acute or severe asthma, hypercarbia, or a paralytic ileus.

SAFETY ALERT

Opioid Analgesics

Morphine can cause respiratory depression, respiratory arrest, cardiac arrest, and shock. Nurses must monitor the client frequently (reassess at least every 5–10 minutes) when using morphine to control pain.

Table 22.3 is a drug prototype table for opioid agonists featuring morphine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Opioid agonist **Mechanism of Action** Primarily a mu opioid receptor agonist that causes modulation of pain in the central and peripheral nervous systems	**Drug Dosage** *For acute myocardial infarction if optimal nitroglycerin does not control chest pain:* 4–8 mg IV initially, then 2–8 mg IV repeated every 5–15 minutes if needed for complete pain relief.
Indications For management of pain not responsive to nonnarcotic analgesics **Therapeutic Effects** Relieves pain	**Drug Interactions** Central nervous system depressants: • Other narcotic analgesics • Phenothiazines • Tricyclic antidepressants • Tranquilizers • Sedatives • Hypnotics • Antiemetics Muscle relaxants Cimetidine Anticholinergics **Food Interactions** Alcohol
Adverse Effects Respiratory depression Respiratory arrest Apnea Circulatory depression Shock Cardiac arrest Sedation Lightheadedness Dizziness Nausea Vomiting Constipation	**Contraindications** Known hypersensitivity to morphine Respiratory depression Acute or severe bronchial asthma or hypercarbia Paralytic ileus

TABLE 22.3 **Drug Prototype Table: Morphine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are receiving morphine for chest pain:

- Place the client on continuous cardiac monitoring.
- Assess the client's vital signs and level of consciousness before administering morphine intravenously.
- Reassess vital signs and level of consciousness frequently after administering morphine intravenously.
- If the client's respiratory rate is less than 10 breaths/min, inform the health care provider.
- Assess the client's pain frequently.
- Reassess the client's pain 15 minutes after administering morphine.
- Ensure that a morphine reversal agent (naloxone) is available.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving morphine for unstable angina or AMI should:

- Alert the nurse if any of these occur:
  - Their chest pain changes (either improves or worsens)
  - They feel sleepy, dizzy, or lightheaded
  - They experience nausea or vomiting

See Pain Response Drugs for full client teaching guidelines on morphine.

FDA BLACK BOX WARNING

Morphine

Life-threatening respiratory depression, addiction, abuse, and misuse can occur with morphine use. Concomitant use of morphine with benzodiazepines or other central nervous system depressants may result in profound sedation and/or respiratory depression.

Dysrhythmia Drugs

There is a saying in cardiac nursing that there are only three problems with the conduction system: The heart can beat too fast, too slow, or not at all.

This is an oversimplification, but each one of these problems can lead to hemodynamic instability and potentially death. Once again, the importance of cardiac output cannot be emphasized enough. Cardiac output is a function of heart rate and stroke volume. If the heart rate is too fast, then ventricular filling cannot occur, and cardiac output is affected. If the heart rate is too slow, then not enough blood will be pumped, and cardiac output is affected. If there is no heart rate at all, then, of course, there is no cardiac output.

The cardiac conduction system—specifically, the SA node—determines the heart rate. The SA node is influenced by the sympathetic and parasympathetic nervous systems. As with all other tissues in the body, it must have a blood supply, and it needs the correct amount of electrolytes (sodium, potassium, calcium, and chloride) to function optimally. The cardiac conduction system (see Figure 22.4) includes the SA node, the AV node, the bundle of His, and the Purkinje fibers.

Although the main pacemaker of the heart is the SA node, other areas of the conduction system generate electrical impulses. The SA node generates impulses at 60–100 beats/min, the AV node at 40–60 beats/min, and the ventricles at 20–40 beats/min. Typically, the conduction system will conduct the fastest rate, which is why the system normally follows the SA node impulses.

Cardiac conduction can be categorized by area of the heart: atrial conduction and ventricular conduction. Most conduction problems in the atria are not life-threatening, but supraventricular tachycardia, atrial fibrillation with rapid ventricular response, and sick sinus syndrome (which can cause hemodynamically unstable bradycardia) can cause hemodynamic instability and potentially death. Ventricular dysrhythmias nearly always cause hemodynamic instability and will lead to death if not treated rapidly. Ventricular dysrhythmias include ventricular tachycardia, pulseless ventricular tachycardia, and ventricular fibrillation.

Emergency dysrhythmias discussed in this chapter include:

- **Asystole**: Complete cessation of electrical activity in the heart
- **Atrial fibrillation with rapid ventricular response**: Rapid electrical stimulation and conduction that cause the atria to have unorganized contraction (fibrillation) and the ventricles to beat rapidly
- **Symptomatic bradycardia**: Heart rate less than 60 beats per minute that negatively affects cardiac output
- **Pulseless electrical activity**: Life-threatening dysrhythmia in which the electrical system conducts impulses but the cardiac myocytes do not respond
- **Pulseless ventricular tachycardia**: Life-threatening dysrhythmia in which the ventricles contract so rapidly that a pulse cannot be detected
- **Supraventricular tachycardia**: Rapid heart rate that originates from above the ventricles
- **Ventricular fibrillation**: Life-threatening dysrhythmia originating in the ventricles in which ventricles are not

coordinated in their contraction, leading to minimal cardiac output

- **Ventricular tachycardia**: Dysrhythmia that originates from the ventricles and causes them to contract rapidly; if it becomes fast enough, it can turn into pulseless ventricular tachycardia, which is life-threatening

The drugs described in this section are used in emergency situations to restore hemodynamic stability and improve cardiac conduction. Antiarrhythmic drugs that are used long term are discussed in Antidysrhythmic Drugs.

Adenosine

Adenosine is a class V antidysrhythmic drug. It is used to convert supraventricular tachycardia into normal sinus rhythm (the regular conduction pattern of the heart). Adenosine affects how potassium and calcium move into and out of the myocardial conduction cells that affect the resting membrane potential, causing conduction to take longer. This is useful in disrupting supraventricular tachycardia and gives the heart the opportunity to restart in normal sinus rhythm.

Adverse Effects and Contraindications

Adenosine may cause flushing of the skin, palpitations, chest pain, hypotension, lightheadedness, nausea, sweating, nervousness, numbness, and apprehension. It decreases conduction through the AV node and may produce short-lasting heart block. It is important to note that the benefit of adenosine in a life-threatening event outweighs the risk of adverse effects.

Contraindications to adenosine include second- or third-degree heart block (except in clients with a pacemaker), sinus node disease (sick sinus syndrome or symptomatic bradycardia), and known hypersensitivity to adenosine.

Table 22.4 is a drug prototype table for adenosine use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Class V antiarrhythmic **Mechanism of Action** Affects potassium and calcium channels in the myocardial conducting cells, significantly slowing heart rate	**Drug Dosage** *For supraventricular tachycardia:* 6 mg rapid IV bolus (administered over 1–2 seconds); if supraventricular tachycardia is not eliminated, administer 12 mg rapid IV bolus. The 12 mg dose may be repeated once if required.
Indications To convert supraventricular tachycardia to normal sinus rhythm **Therapeutic Effects** Slows nerve impulses in the heart	**Drug Interactions** Methylxanthines (caffeine, theophylline) Dipyridamole Carbamazepine **Food Interactions** Caffeine
Adverse Effects Flushing of skin Palpitations Chest pain Hypotension Lightheadedness Nausea Sweating Nervousness Numbness Apprehension Short-lasting heart block due to decreased conduction through the AV node	**Contraindications** Second- or third-degree heart block (except in clients with a pacemaker) Sinus node disease (sick sinus syndrome or symptomatic bradycardia) Known hypersensitivity to adenosine

TABLE 22.4 **Drug Prototype Table: Adenosine** (sources: https://dailymed.nlm.nih.gov/dailymed/; Singh & McKintosh, 2022)

CLINICAL TIP

Adenosine

Adenosine has a very short half-life and should be administered as a rapid IV bolus directly into a vein, followed by a rapid saline flush.

Nursing Implications

The nurse should do the following for clients who are receiving adenosine intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor vital signs frequently.
- Administer adenosine as an IV push directly into a vein over 1–2 seconds.
- Administer a rapid saline bolus immediately after administering adenosine.
- Be prepared to administer a second dose.
- If the client is alert, inform them that they may feel chest pain once the bolus is given. The chest pain should subside quickly (in less than 1 minute).
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

In supraventricular tachycardia, the client may not be conscious because of decreased cardiac output.

If alert and oriented, the client receiving adenosine should:

- Inform the health care team if they have a known heart block or sick sinus syndrome.

Amiodarone

Amiodarone is a class III antiarrhythmic drug used for hemodynamically unstable ventricular tachycardia, ventricular fibrillation, and other dysrhythmias. It blocks potassium and calcium channels from opening, which slows down cardiac conduction and therefore slows heart rate. Antidysrhythmic Drugs covers the use of amiodarone in the management of chronic dysrhythmias.

Adverse Effects and Contraindications

Amiodarone can cause hypotension, bradycardia, atrioventricular block, hepatic injury, heart rhythm disturbances, pulmonary injury, loss of vision, thyroid injury, hypersensitivity, anorexia, nausea, vomiting, and photosensitivity. It is important to note that the benefit of amiodarone in a life-threatening event outweighs the risk of adverse effects.

Contraindications to amiodarone include known hypersensitivity, cardiogenic shock, marked sinus bradycardia, and second- or third-degree AV block (unless the client has an implanted pacemaker).

Table 22.5 is a drug prototype table for amiodarone use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Class III antiarrhythmic **Mechanism of Action** Blocks potassium and calcium channels in the cardiac conducting cells, slowing the heart rate	**Drug Dosage** *For hemodynamically unstable ventricular tachycardia or ventricular fibrillation:* 150 mg IV bolus given over 10 minutes, then 360 mg IV infused over the next 6 hours, then 540 mg IV infused over the next 18 hours; dosage should be titrated after 24 hours.
Indications For ventricular fibrillation and hemodynamically unstable ventricular tachycardia **Therapeutic Effects** Slows nerve impulses in the heart	**Drug Interactions** Drugs that prolong the QT interval (increased risk of torsade de pointes): • Class I antiarrhythmics • Class III antiarrhythmics • Lithium • Phenothiazines • Tricyclic antidepressants Digoxin (increases effect) Warfarin (increases effect) HMG-CoA reductase inhibitors/statin drugs (increases effect; risk of myopathy) Protease inhibitors St. John's wort **Food Interactions** Grapefruit/grapefruit juice
Adverse Effects Anorexia Nausea and vomiting Hypotension Bradycardia and atrioventricular block Hepatic injury Dysrhythmias Photosensitivity Pulmonary injury Loss of vision Thyroid injury Hypersensitivity	**Contraindications** Known hypersensitivity Cardiogenic shock Marked sinus bradycardia Second- or third-degree AV block (unless the client has an implanted pacemaker)

TABLE 22.5 **Drug Prototype Table: Amiodarone** (sources: https://dailymed.nlm.nih.gov/dailymed/; Florek & Girsadas, 2022)

SAFETY ALERT

Amiodarone

Amiodarone can cause pulmonary toxicity and swelling in the lungs.

Nursing Implications

The nurse should do the following for clients who are receiving amiodarone intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor vital signs frequently.
- Monitor level of consciousness.
- Monitor laboratory values and report abnormal findings to the health care provider.
- Have resuscitative equipment and drugs immediately available.
- Monitor for adverse effects of amiodarone infusion.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving amiodarone should:

- Inform the health care provider of nausea, which may be an early indication of liver damage.

Clients with ventricular fibrillation or hemodynamically unstable ventricular tachycardia are typically no longer conscious. See Antidysrhythmic Drugs for client teaching guidelines for amiodarone in less acute situations.

FDA BLACK BOX WARNING

Amiodarone

Amiodarone can cause pulmonary toxicity and swelling in the lungs.

Atropine

Atropine is a first-line drug used for treating symptomatic bradycardia. It is an **anticholinergic** drug, which means it blocks receptors in the parasympathetic nervous system. The heart is constantly stimulated by both the parasympathetic nervous system (PNS) and the sympathetic nervous system (SNS). It reacts to whichever system is sending more impulses. If the PNS signals are blocked, then the heart receives fewer signals from acetylcholine, the primary neurotransmitter of the PNS. Because of fewer signals from the PNS, the SNS signaling is stronger, which increases the heart rate.

Adverse Effects and Contraindications

Atropine can cause tachycardia, acute glaucoma, pyloric obstruction, and complete urinary retention. It is important to note that the benefit of atropine in a life-threatening event outweighs the risk of adverse effects.

There are no contraindications to the use of atropine.

Table 22.6 is a drug prototype table for atropine use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anticholinergic **Mechanism of Action** Inhibits cholinergic nerves, resulting in decreased parasympathetic stimulation	**Drug Dosage** *For symptomatic bradycardia:* 1 mg IV every 3–5 minutes; maximum dose: 3 mg.
Indications Symptomatic bradycardia Treatment of organophosphorus poisoning **Therapeutic Effects** Increased heart rate	**Drug Interactions** Mexiletine **Food Interactions** No significant interactions
Adverse Effects Tachycardia Acute glaucoma Pyloric obstruction Complete urinary retention	**Contraindications** None

TABLE 22.6 **Drug Prototype Table: Atropine** (sources: https://dailymed.nlm.nih.gov/dailymed/; McLendon & Preuss, 2022)

Nursing Implications

The nurse should do the following for clients receiving atropine intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor vital signs frequently.
- Monitor level of consciousness.
- Have resuscitative equipment and drugs available.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

In symptomatic bradycardia, the client may not be conscious because of decreased cardiac output.

If alert and oriented, the client receiving atropine should:

- Inform the health care team if they feel different (better or worse) after the initial dose.
- Inform the health care team if they feel a fast heart rate or racing heart after the dose.

Diltiazem

Diltiazem is a nondihydropyridine **Calcium channel blocker** and a class IV antiarrhythmic drug. Nondihydropyridine calcium channel blockers inhibit calcium flow into cardiac myocytes, which results in decreased force of contractions and decreased heart rate. Therefore, diltiazem is useful for treating supraventricular tachycardia and atrial fibrillation with rapid ventricular response. In addition, calcium channel blockers cause vasodilation and can reduce blood pressure. Antihypertensive and Antianginal Drugs discusses the use of calcium channel blockers in hypertension.

Adverse Effects and Contraindications

Diltiazem can cause asystole; atrial flutter; first-, second-, and third-degree atrioventricular block; bradycardia; chest pain; congestive heart failure; sinus pause; sinus node dysfunction; syncope; ventricular dysrhythmia; ventricular fibrillation; ventricular tachycardia; dizziness; allergic reaction; Stevens–Johnson syndrome; and angioedema. It is important to note that the benefit of diltiazem in a life-threatening event outweighs the risk of adverse effects.

Contraindications include sick sinus syndrome, unless the client has a pacemaker; second- or third-degree heart block, unless the client has a pacemaker; severe hypotension and/or cardiogenic shock; hypersensitivity; ventricular tachycardia; and AMI.

Diltiazem should not be administered concurrently with IV beta-adrenergic blockers.

Table 22.7 is a drug prototype table for diltiazem use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nondihydropyridine calcium channel blocker; class IV antiarrhythmic drug **Mechanism of Action** Inhibits calcium ions from entering the cell, resulting in decreased force of cardiac contraction and vascular smooth muscle relaxation	**Drug Dosage** *For paroxysmal supraventricular tachycardia or atrial fibrillation with rapid ventricular response:* 0.25 mg/kg actual body weight IV bolus over 2 minutes. If response inadequate, 0.35 mg/kg actual body weight IV bolus administered over 2 minutes. Subsequent bolus doses may be administered as needed according to the health care provider's discretion. After initial bolus(es), continuous IV infusion may be needed, starting at 10 mg/hour for up to 24 hours.
Indications Atrial fibrillation with rapid ventricular response Supraventricular tachycardia **Therapeutic Effects** Slows heart rate Lowers blood pressure	**Drug Interactions** Beta-adrenergic blockers may increase incidence of bradycardia **Food Interactions** Alcohol
Adverse Effects Allergic reaction Angioedema Asystole Atrial flutter First-degree atrioventricular block Second-degree atrioventricular block Third-degree atrioventricular block Bradycardia Chest pain Congestive heart failure Hypotension Sinus pause Sinus node dysfunction Syncope Ventricular dysrhythmia Ventricular fibrillation Ventricular tachycardia Dizziness Stevens–Johnson syndrome	**Contraindications** Sick sinus syndrome (unless client has pacemaker) Second- or third-degree heart block (unless client has pacemaker) Severe hypotension and/or cardiogenic shock Hypersensitivity Ventricular tachycardia Acute myocardial infarction

TABLE 22.7 **Drug Prototype Table: Diltiazem** (sources: https://dailymed.nlm.nih.gov/dailymed/; Talreja & Cassagnol, 2022)

Nursing Implications

The nurse should do the following for clients receiving diltiazem intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor blood pressure frequently.
- Monitor level of consciousness.
- Have resuscitative equipment and drugs available.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

In supraventricular tachycardia or atrial fibrillation with rapid ventricular response, the client may not be conscious because of decreased cardiac output.

If alert and oriented, the client receiving diltiazem should:

- Inform the health care team if they have a known heart block or sick sinus syndrome.

See Antidysrhythmic Drugs for client teaching guidelines for diltiazem in less acute situations.

Epinephrine

Epinephrine (adrenaline) is a hormone that stimulates the SNS during the fight-or-flight response. SNS stimulation results in a faster heart rate, increased cardiac output, and pulmonary dilation (for increased oxygen intake), among other things. Epinephrine is a nonselective **adrenergic agonist**, which means it stimulates all receptors in the SNS. Epinephrine is used in a variety of emergency situations. In cardiac emergencies, epinephrine is used in ventricular fibrillation, pulseless ventricular tachycardia, asystole, and pulseless electrical activity.

Adverse Effects and Contraindications

Epinephrine can cause anxiety and excitability, headache, fear, heart palpitations, tachycardia, supraventricular tachycardia, ventricular arrhythmias, hypertension, cerebral hemorrhage, hemiplegia, subarachnoid hemorrhage, anginal pain in clients with angina, pulmonary edema, hypoglycemia, hypokalemia, and lactic acidosis. It is important to note that the benefit of epinephrine in a life-threatening event outweighs the risk of adverse effects.

Contraindications to epinephrine include cardiac dilation, coronary artery insufficiency, and shock during general anesthesia. Epinephrine contains sodium bisulfate, which may cause an allergic reaction.

Table 22.8 is a drug prototype table for epinephrine use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Adrenergic agonist (nonselective) **Mechanism of Action** Binds to sympathetic nervous system receptors and stimulates the sympathetic nervous system, which causes increased heart rate, increased blood pressure, and increased oxygen intake in the lungs	**Drug Dosage** *For ventricular fibrillation, pulseless ventricular tachycardia, asystole, and pulseless electrical activity:* 0.1–1 mg IV bolus (using 0.1 mg/mL concentration) repeated every 5 minutes as necessary during cardiac resuscitation. *For anaphylaxis:* 0.3–0.5 mg intramuscularly (using 1 mg/mL concentration), repeated every 5–10 minutes as needed.
Indications Emergency treatment of type I hypersensitivity reactions (anaphylaxis), ventricular fibrillation, pulseless ventricular tachycardia, asystole, and pulseless electrical activity Emergency treatment of anaphylaxis **Therapeutic Effects** Increases heart rate Increases blood pressure Bronchodilation	**Drug Interactions** Other sympathomimetic (adrenergic stimulant) drugs such as isoproterenol Digoxin Other medications may potentiate the effects: • Tricyclic antidepressants • Antihistamines • Sodium l-thyroxine • Beta-adrenergic blockers Rapidly acting nitrates or alpha-blocking agents (may counteract epinephrine's effects) Use with caution in clients taking monoamine oxidase inhibitors **Food Interactions** No significant interactions
Adverse Effects Anxiety Excitability Headache Fear Heart palpitations Tachycardia Supraventricular tachycardia Ventricular arrhythmias Myocardial ischemia Hypertension Cerebral hemorrhage Hemiplegia Subarachnoid hemorrhage Anginal pain in clients with angina Pulmonary edema Hypoglycemia Hypokalemia Lactic acidosis	**Contraindications** Cardiac dilation Coronary artery insufficiency Shock during general anesthesia

TABLE 22.8 **Drug Prototype Table: Epinephrine** (sources: https://dailymed.nlm.nih.gov/dailymed/; Dalal & Grujic, 2022; McLendon & Sternard, 2022; Smith & Maani, 2022)

Nursing Implications

The nurse should do the following for clients receiving epinephrine intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor blood pressure frequently. (Often, blood pressure is measured continuously when client is in shock.)
- Monitor level of consciousness.

- Have resuscitative equipment and drugs available.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

In ventricular fibrillation, pulseless ventricular tachycardia, asystole, or pulseless electrical activity, the client will be unconscious. In anaphylaxis, the client may be unconscious.

If alert and oriented, the client receiving epinephrine should:

- Inform the health care team if they have a change in status (better or worse) after medication administration.
- Inform the health care team if they notice a change in their breathing.

Lidocaine

Lidocaine is classified as a local anesthetic agent, but it is also a class Ib antiarrhythmic drug used in acute ventricular dysrhythmias. Lidocaine blocks sodium channels, which slows the cardiac action potential and causes the electrical stimulation threshold to be higher. The higher stimulation threshold causes the cardiac conduction cells to be less likely to conduct action potentials, which ultimately treats ventricular tachyarrhythmias.

Adverse Effects and Contraindications

Lidocaine can cause respiratory depression and arrest, unconsciousness, convulsions, tremors, twitching, vomiting, blurred or double vision, drowsiness, dizziness, light-headedness, agitation, confusion, paresthesia, and dysarthria. It is important to note that the benefit of lidocaine in a life-threatening event outweighs the risk of adverse effects.

Contraindications to lidocaine include a history of hypersensitivity, Stokes–Adams syndrome, Wolff–Parkinson–White syndrome, and heart block.

Table 22.9 is a drug prototype table for lidocaine use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications. Lidocaine as a topical anesthetic is not addressed in this section.

Drug Class Class Ib antiarrhythmic **Mechanism of Action** Blocks sodium channels in cardiac conducting cells, which ultimately causes slowed conduction and decreased heart rate	**Drug Dosage** *For ventricular arrhythmias:* 1–1.5 mg/kg IV bolus at 25–50 mg/min. Continuous IV infusion may be needed; usual dosing is 1–4 mg/min.
Indications Emergency management of ventricular arrhythmias **Therapeutic Effects** Decreases heart rate	**Drug Interactions** Other antiarrhythmic drugs (cardiac effects may be additive or antagonistic, which may lead to toxic effects) Propranolol, metoprolol, nadolol (increase the serum concentration of lidocaine) **Food Interactions** No significant interactions
Adverse Effects Respiratory depression Respiratory arrest Unconsciousness Convulsions Tremors Twitching Vomiting Blurred or double vision Drowsiness Dizziness Light-headedness Agitation Confusion Cardiovascular arrest Bradycardia, which may lead to cardiovascular arrest Hypotension Ventricular fibrillation Ventricular tachycardia Asystole Allergic reaction, including anaphylaxis	**Contraindications** History of known reaction Stokes–Adams syndrome Wolff–Parkinson–White syndrome Severe sinoatrial heart block Severe atrioventricular heart block Severe intraventricular heart block

TABLE 22.9 **Drug Prototype Table: Lidocaine** (sources: https://dailymed.nlm.nih.gov/dailymed/; Al-Khatib et al., 2018; Beecham et al., 2022; Klabunde, 2022)

Nursing Implications

The nurse should do the following for clients receiving lidocaine intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor blood pressure frequently.
- Monitor level of consciousness.
- Have resuscitative equipment and drugs available.
- For continuous IV lidocaine infusion, closely monitor the rate and provide continuous ECG monitoring.
- Monitor for adverse effects of lidocaine infusion
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving lidocaine should:

- Inform the health care provider of tremors, twitching, nausea, vomiting, blurred or double vision, dizziness, lightheadedness, or confusion.

In acute ventricular arrhythmias, clients are typically no longer conscious. See Antidysrhythmic Drugs for client teaching guidelines for lidocaine in less acute situations.

Procainamide

Procainamide is a class Ia antiarrhythmic drug that binds to sodium channels, reducing the speed of conduction. It is used in life-threatening ventricular arrhythmias.

Adverse Effects and Contraindications

Procainamide can cause hypotension, asystole, ventricular fibrillation, lupus erythematosus–like syndrome, pleural effusions, pericarditis, neutropenia, thrombocytopenia, hemolytic anemia, agranulocytosis, dizziness, weakness, and elevated liver enzyme levels.

Prolonged use of procainamide often leads to a positive antinuclear antibody (ANA) test; if this occurs, the risk–benefit ratio of procainamide use should be reassessed. It is important to note that the benefit of procainamide in a life-threatening event generally outweighs the risk of adverse effects.

Contraindications to the use of procainamide include a history of hypersensitivity, complete heart block, atrial fibrillation or flutter, congestive heart failure, lupus erythematosus, torsade de pointes, myasthenia gravis, and sulfite sensitivity.

Table 22.10 is a drug prototype table for procainamide use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Class Ia antiarrhythmic **Mechanism of Action** Antagonizes cardiac cell sodium channels, which ultimately slows the heart rate	**Drug Dosage** *For life-threatening ventricular arrhythmias:* Loading dose 10–17 mg/kg at a rate of 20–50 mg/min. Maintenance therapy may be indicated; dosing is variable.
Indications Emergency management of ventricular arrhythmias **Therapeutic Effects** Decreases heart rate	**Drug Interactions** Digitalis derivatives Other class Ia antiarrhythmic drugs Other antiarrhythmic drugs (may prolong the QT interval) **Food Interactions** No significant interactions
Adverse Effects Hypotension Asystole Ventricular fibrillation Lupus erythematosus–like syndrome Pleural effusion Pericarditis Neutropenia Thrombocytopenia Hemolytic anemia Agranulocytosis Dizziness Weakness Elevated liver enzyme levels	**Contraindications** History of hypersensitivity Complete heart block Atrial fibrillation or flutter Congestive heart failure Lupus erythematosus Torsade de pointes Myasthenia gravis Sulfite sensitivity

TABLE 22.10 **Drug Prototype Table: Procainamide** (sources: https://dailymed.nlm.nih.gov/dailymed/; Pritchard & Thompson, 2023)

Nursing Implications

The nurse should do the following for clients receiving procainamide intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor blood pressure frequently.
- Monitor level of consciousness.
- Have other resuscitative equipment and drugs available.
- Monitor laboratory values, including ANA titer and liver enzyme levels, and report abnormal results to the health care provider
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving procainamide should:

- Inform the health care provider of generalized rheumatic pain, dizziness, or weakness.

In acute ventricular arrhythmias, clients are typically no longer conscious. See Antidysrhythmic Drugs for client teaching guidelines for procainamide in less acute situations.

FDA BLACK BOX WARNING

Procainamide

Prolonged administration of procainamide often leads to the development of a positive antinuclear antibody (ANA) test, with or without symptoms of a lupus erythematosus–like syndrome. If a positive ANA titer develops, the benefit versus risks of continued procainamide therapy should be assessed.

Dopamine and Dobutamine

After a cardiac event, clients often may still have hypotension or be in shock even after the immediate emergency is over. They may need medications to stabilize their blood pressure so that tissues are perfused. Dopamine and dobutamine are two drugs that help achieve and maintain hemodynamic stability.

Dopamine

Endogenous (naturally occurring in the body) dopamine is a hormone that plays a role in stimulating the SNS. Dopamine, an **inotropic agent**, is converted into epinephrine within the bloodstream. Dopamine binds to alpha-1, alpha-2, beta-1, and dopaminergic receptors. Adrenergic stimulation of alpha-1 and alpha-2 receptors causes vasoconstriction, which leads to increased blood pressure. Adrenergic stimulation of beta-1 receptors directly increases the heart rate.

Exogenous (synthetic) dopamine mimics the body's own dopamine to the same effect. Dopamine is used in profound hypotension and shock to increase cardiac output by increasing the rate and force of contraction and blood pressure by vasoconstriction. At low doses (0.5–2 mcg/kg/min), dopamine causes vasodilation and can be used to increase urinary output. At intermediate doses (2–10 mcg/kg/min), it increases heart rate and stroke volume, which leads to increased cardiac output. At high doses, dopamine causes vasoconstriction, which increases blood pressure.

Adverse Effects and Contraindications

Dopamine can cause ventricular arrhythmia, atrial fibrillation, ectopic beats, tachycardia, anginal pain, palpitations, cardiac conduction abnormalities, widened QRS complex, bradycardia, hypotension, hypertension, vasoconstriction, dyspnea, azotemia, headache, and anxiety. Extravasation of dopamine into the tissue around an IV site may cause necrosis, sloughing, and potentially gangrene. It is important to note that the benefit of dopamine in a life-threatening event outweighs the risk of adverse effects.

Contraindications to the use of dopamine include pheochromocytoma, uncorrected tachyarrhythmias or ventricular fibrillation, and allergy to metabisulfite.

SAFETY ALERT

Dopamine

Dopamine may cause peripheral ischemia in clients with a history of occlusive vascular disease.

Dopamine is a potent drug. It should be administered only in an intensive care area with proper monitoring available.

Table 22.11 is a drug prototype table for dopamine use in emergency situations. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Inotrope **Mechanism of Action** Converts to epinephrine in the bloodstream, which ultimately causes vasoconstriction and increased rate and force of contraction	**Drug Dosage** *For hemodynamic instability:* Initiate titration at 2–5 mcg/kg/min and titrate as directed by health care provider. Titration parameters include blood pressure and signs of tissue perfusion (adequate urine output).
Indications Emergency management of hypotension and shock **Therapeutic Effects** Increases heart rate	**Drug Interactions** Monoamine oxidase inhibitors Tricyclic antidepressants Beta-adrenergic blockers (may antagonize the effects) Alpha-adrenergic blockers (may antagonize the effects) Haloperidol Cyclopropane or halogenated hydrocarbon anesthetics Other vasopressors and oxytocic drugs Phenytoin **Food Interactions** No significant interactions
Adverse Effects Ventricular arrhythmia Atrial fibrillation Ectopic beats Tachycardia Anginal pain Palpitations Cardiac conduction abnormalities Widened QRS complex Bradycardia Hypotension Hypertension Vasoconstriction Dyspnea Azotemia Headache Anxiety	**Contraindications** Pheochromocytoma Uncorrected tachyarrhythmias or ventricular fibrillation Allergy to metabisulfite

TABLE 22.11 **Drug Prototype Table: Dopamine** (sources: https://dailymed.nlm.nih.gov/dailymed/; Sonne et al., 2023)

Nursing Implications

The nurse should do the following for clients receiving dopamine intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor blood pressure frequently.
- Monitor level of consciousness.
- Have resuscitative equipment and drugs available.
- Monitor IV site for signs of extravasation.
- Monitor for signs and symptoms of occlusive vascular disease.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

In hypotension or shock, the client may be unconscious.

If the client receiving dopamine is alert and oriented, the client should:

- Inform the health care team if they have a change in status (better or worse) after medication administration.
- Inform the heath care team if they have pain at the IV site.
- Inform the health care team if they have a headache.

FDA BLACK BOX WARNING

Dopamine

Dopamine may cause peripheral ischemia in clients with a history of occlusive vascular disease.

Dobutamine

Dobutamine is a beta-1 adrenergic agonist that stimulates the heart to contract more forcefully and, to a lesser extent, faster. It is used for the cardiac decompensation that can occur immediately after a cardiac event.

Adverse Effects and Contraindications

Dobutamine can cause increased heart rate, increased blood pressure, ventricular ectopic activity, hypotension, and IV site reaction. It is important to note that the benefit of dobutamine in a life-threatening event outweighs the risk of adverse effects.

Contraindications to the use of dobutamine include idiopathic hypertrophic subaortic stenosis and hypersensitivity to bisulfite. Use after AMI may be contraindicated because of increased contractility. Dobutamine may cause marked increase in blood pressure or heart rate. Hypovolemia must be corrected prior to initiating dobutamine.

CLINICAL TIP

Dobutamine

Dobutamine should not be mixed with any other drug in the same solution because it is incompatible with many other drugs.

Table 22.12 is a drug prototype table for dobutamine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Inotrope **Mechanism of Action** Directly stimulates beta-1 receptors in the heart, which increases contractility and heart rate	**Drug Dosage** *For hemodynamic instability:* Initiate titration at 0.5–1 mcg/kg/min; titrate based on client response, including blood pressure and urine output.
Indications Short-term inotropic support for cardiac decompensation **Therapeutic Effects** Increases contractility Increases heart rate	**Drug Interactions** Beta-adrenergic blockers (may reduce the effectiveness of dobutamine) Sodium bicarbonate Alkaline solutions **Food Interactions** No significant interactions
Adverse Effects Increased heart rate Increased blood pressure Ventricular ectopic activity Hypotension IV site reaction	**Contraindications** Idiopathic hypertrophic subaortic stenosis Hypersensitivity to bisulfite

TABLE 22.12 **Drug Prototype Table: Dobutamine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients receiving dobutamine intravenously:

- Place the client on continuous cardiac monitoring.
- Monitor blood pressure frequently.
- Monitor level of consciousness.
- Have resuscitative equipment and drugs available.
- Ensure that dobutamine is not mixed with any other drug in the same solution.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving dobutamine should:

- Inform the health care team if any of these occur:
  - They have a change in status (better or worse) after medication administration.
  - They notice chest pain; dyspnea; or numbness, tingling, or burning in their extremities.
  - They have discomfort or pain at the IV site.

General Nursing Implications for Cardiac Emergencies and Anaphylaxis

In the emergency department and critical care unit, nurses are current in cardiopulmonary resuscitation (CPR), advanced cardiac life support (ACLS), advanced trauma life support (ATLS), and other emergency certifications. Many nurses undergo certified emergency nurse (CEN) or certified critical care nurse (CCRN) certification. Advanced training for cardiac and other emergencies is helpful in a fast-paced, stressful environment.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

James Ryan is a 72-year-old client whose wife brought him to the emergency department because of chest pain and difficulty breathing. He said he was shoveling snow from the sidewalk when he started having pain in his left arm

and chest. He also had difficulty catching his breath. After a few minutes, James went inside and sat down, but the pain in his arm and chest continued. He started to feel lightheaded, and even though he was sitting down, he still found it hard to breathe. James wanted to lie down on the couch, but his wife insisted that he go to the emergency department.

History
Hypertension

Current Medications
Losartan 50 mg daily
Hydrochlorothiazide 25 mg daily

Vital Signs		Physical Examination
Temperature:	98.1°F	• *Head, eyes, ears, nose, throat (HEENT):* Within defined limits • *Neurologic:* Within defined limits • *Cardiovascular:* No jugular venous distension; S1 and S2 heard on heart auscultation; no S3 noted; brisk capillary refill in nailbeds of hands and feet • *Respiratory:* Clear to auscultation bilaterally • *GI:* Bowel sounds heard in all four quadrants, no tenderness, no distension • *GU:* Appropriate for age • *Integumentary:* Skin appropriate for age
Blood pressure:	160/92 mm Hg	
Heart rate:	86 beats/min	
Respiratory rate:	20 breaths/min	
Oxygen saturation:	96% on room air	
Height:	5'11"	
Weight:	240 lb	

TABLE 22.13

In the emergency department, James underwent an ECG and bloodwork, which revealed he was in the midst of an AMI.

1. The nurse receives orders to administer nitroglycerin sublingually. Which parameter will the nurse monitor to determine the effectiveness of nitroglycerin?
   a. Chest pain
   b. Heart rate
   c. Blood pressure
   d. Level of consciousness

2. The health care provider orders aspirin for James. Which action should the nurse take?
   a. Tell James not to chew the aspirin.
   b. Tell James that aspirin will relieve his pain.
   c. Ask James if he has a history of asthma.
   d. Teach James that aspirin causes vasodilation.

22.3 Shock Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 22.3.1 Identify the characteristics of drugs used to treat anaphylactic, hypovolemic, and cardiogenic shock.
- 22.3.2 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat anaphylactic, hypovolemic, and cardiogenic shock.
- 22.3.3 Describe nursing implications of drugs used to treat anaphylactic, hypovolemic, and cardiogenic shock.
- 22.3.4 Explain the client education related to drugs used to treat anaphylactic, hypovolemic, and cardiogenic shock.

Shock is a state of medical emergency in which tissues are not receiving enough oxygenated blood to sustain life. If not treated rapidly, decreased perfusion will cause hypoxia and eventually cell and tissue death. Because many different cells and tissues are at risk, cell and tissue death can lead to multiorgan failure and, eventually, death.

Anaphylactic Shock Drugs

Anaphylactic shock is a severe and life-threatening response to an allergen to which the body has a hypersensitivity. Typically, systemic vasodilation occurs, which causes shock and bronchoconstriction (often severe). Drugs are used to reverse bronchoconstriction and support hemodynamic stability.

Epinephrine

Epinephrine, a nonselective adrenergic agonist, is the most important drug used to treat anaphylactic shock. It causes sympathetic nervous system stimulation, which dilates the pulmonary bronchioles to open up airways and constricts blood vessels to increase blood pressure. Epinephrine acts very quickly and can decrease bronchoconstriction within 3–5 minutes. Epinephrine can be administered intramuscularly or intravenously depending on the acuteness of the situation. Table 22.8 earlier in the chapter is a drug prototype table for epinephrine use in emergency situations.

Nursing Implications

The nurse should do the following for clients receiving epinephrine intramuscularly or intravenously for anaphylactic shock:

- Place the client on continuous cardiac monitoring.
- Assess lung sounds prior to administration and frequently after administration.
- Monitor blood pressure frequently. (Blood pressure is often measured continuously when a client is in shock.)
- Monitor respiratory rate frequently.
- Monitor oxygen saturation continuously.
- Monitor level of consciousness.
- Have resuscitative equipment and drugs available.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

In ventricular fibrillation, pulseless ventricular tachycardia, asystole, or pulseless electrical activity, the client will be unconscious. In anaphylaxis, the client may be unconscious.

If alert and oriented, the client receiving epinephrine should:

- Inform the health care team if they have a change in status (better or worse) after medication administration.
- Inform the health care team if they notice a change in their breathing.

Albuterol

Albuterol is a beta-adrenergic receptor agonist that causes bronchiole smooth muscle dilation, which opens up the

bronchiole airways. Albuterol may be used in anaphylaxis if epinephrine does not fully open the airways. In anaphylaxis, it is administered as an inhaled nebulizer treatment.

Adverse Effects and Contraindications

Albuterol can cause paradoxical bronchospasm, tachycardia, and an immediate hypersensitivity reaction.

Hypersensitivity is the only contraindication to albuterol.

Table 22.14 is a drug prototype table for albuterol. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Beta-adrenergic receptor agonist **Mechanism of Action** Directly stimulates beta receptors in the lungs, which causes smooth muscle dilation and opens airways	**Drug Dosage** *For acute/severe bronchospasm:* 2.5–5 mg via nebulizer every 20 minutes for 3 cycles; may repeat treatments every 1–4 hours as needed.
Indications Relief of bronchospasm **Therapeutic Effects** Causes bronchodilation	**Drug Interactions** Other short-acting sympathomimetic aerosol bronchodilators Epinephrine Monoamine oxidase inhibitors Tricyclic antidepressants Beta blockers **Food Interactions** No significant interactions
Adverse Effects Paradoxical bronchospasm Tachycardia Immediate hypersensitivity reaction	**Contraindications** Hypersensitivity

TABLE 22.14 **Drug Prototype Table: Albuterol** (sources: https://dailymed.nlm.nih.gov/dailymed/; Johnson et al., 2023)

Nursing Implications

The nurse should do the following for clients receiving albuterol via nebulizer for anaphylaxis:

- Assess lung sounds prior to administration and frequently after administration.
- Monitor blood pressure frequently. (Blood pressure is often measured continuously when a client is in shock.)
- Monitor respiratory rate frequently.
- Monitor oxygen saturation continuously.
- Monitor level of consciousness.
- Have resuscitative equipment and drugs available.
- Provide client teaching regarding nebulizer treatment.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving albuterol should:

- Hold the nebulizer mouthpiece between their teeth with their lips closed around it.
- Hold the nebulizer in an upright position.
- Understand that treatment often lasts 10–15 minutes.
- Inform the health care provider of chest pain or pressure or a feeling of rapid heart rate.

Isotonic Intravenous Solution

Anaphylactic shock causes fluids to shift from within the blood vessels (intravascular) to the tissues (extravascular).

This can occur very rapidly and is the primary cause of the shock. Isotonic IV solutions have the same amount of sodium concentration as blood does.

Because fluid has shifted to the extravascular space in anaphylactic shock, there is not enough volume in the intravascular space to maintain blood pressure and tissue perfusion. Isotonic intravenous solution will increase volume, which then increases blood pressure.

In anaphylactic shock, 1–2 L of an isotonic IV solution such as normal saline should be administered rapidly (at the highest flow rate possible) as soon as an IV is established. After the initial IV fluid bolus, the client may need continuous IV fluids at a rapid rate to maintain blood pressure. Examples of isotonic IV solutions are normal saline and lactated Ringer's.

Hypovolemic Shock Drugs

Hypovolemic shock occurs when the circulating volume of fluid has decreased so much that it affects tissue perfusion. The first priority in hypovolemic shock is to correct the underlying cause; for example, if the hypovolemia is caused by blood loss, measures should be taken to stop the blood loss, and the client should receive a blood transfusion as soon as possible. Intravenous fluid resuscitation is also used to increase cardiac output and stabilize blood pressure. The use of vasopressors (drugs that increase blood pressure) in hypovolemic shock is controversial and will not be included in this section.

In hypovolemic shock, 2 L of an isotonic IV solution should be administered as quickly as possible. After the initial fluid bolus, additional IV solution may be ordered to maintain blood pressure.

Cardiogenic Shock Drugs

Cardiogenic shock occurs when the myocardium is not able to pump effectively enough to maintain cardiac output. This can be due to ischemia, infarction, or other causes. Cardiogenic shock is treated with vasopressors and SNS stimulation. Cardiac output must be increased in order to restore adequate tissue perfusion. Medications used in cardiogenic shock include dopamine, dobutamine, and norepinephrine. Dopamine and dobutamine are covered in a previous section in this chapter. Norepinephrine can be used for other types of shock, but it is included here because of its effects on the heart.

Norepinephrine

Norepinephrine is an alpha-1 receptor agonist and a moderate beta-1 receptor agonist. Alpha-1 receptors are located in the smooth muscle around blood vessels. When these receptors are stimulated, they cause muscle contraction, which causes vasoconstriction. Beta-1 receptors are located in the heart; when they are stimulated, they cause increased heart rate and force of contraction.

Adverse Effects and Contraindications

Norepinephrine can cause cardiac arrhythmias, severe peripheral ischemia in clients who are hypovolemic, gangrene in clients with occlusive or thrombotic vascular disease (in high doses), and rebound hypotension after discontinuation. Norepinephrine may cause decreased sensitivity to insulin, so clients with diabetes may need their glucose levels monitored more frequently as well as increased doses of antidiabetic medications.

Extravasation of norepinephrine at the IV site can cause tissue necrosis.

There are no contraindications for norepinephrine.

Table 22.15 is a drug prototype table for norepinephrine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Alpha/beta antagonist **Mechanism of Action** Stimulates alpha- and beta-adrenergic receptors, thereby increasing blood pressure, heart rate, and force of contraction	**Drug Dosage** *For profound hypotension or shock:* Initial dose: 8–12 mcg/min, titrated to blood pressure. Typical maintenance dose: 2–4 mcg/min. Hypovolemia must be corrected before initiating norepinephrine infusion.
Indications Severe acute hypotension Shock **Therapeutic Effects** Increased blood pressure Increased heart rate and force of contraction	**Drug Interactions** Monoamine oxidase inhibitors (can lead to profound hypertension) Tricyclic antidepressants (can lead to profound hypertension) Halogenated anesthetics (can cause ventricular tachycardia or fibrillation) **Food Interactions** Caffeine
Adverse Effects Tissue ischemia in clients who are hypovolemic (severe peripheral ischemia) Gangrene in clients with occlusive or thrombotic vascular disease (in high doses) Rebound hypotension after discontinuation Cardiac arrhythmias	**Contraindications** None

TABLE 22.15 **Drug Prototype Table: Norepinephrine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients receiving norepinephrine:

- Place the client on continuous cardiac monitoring.
- Monitor heart rate frequently.
- Monitor level of consciousness.
- Have resuscitative equipment and drugs available.
- Assess the IV site frequently.
- Correct hypovolemia before giving norepinephrine.
- Provide client teaching regarding the drug. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client receiving norepinephrine should:

- Inform the health care team if they have a change in status (better or worse) after medication administration.
- Inform the health care team if they have discomfort or pain at the IV site.

Chapter Summary

This chapter focused on cardiac emergency and shock drugs. Cardiac emergencies can arise from problems within the heart's electrical system or mechanical system and include AMI, unstable angina, and dysrhythmias. Both conduction problems and mechanical problems can affect cardiac output and become life-threatening. Shock, decreased tissue perfusion that can cause injury and death, is also life-threatening.

Common cardiac emergency and shock drugs were presented. Medications used include nitrates, opioid agonists, multiple types of antiarrhythmic drugs, adrenergic agonists, anticholinergics, and intravenous fluids to increase intravascular volume in a client in shock.

Key Terms

acute myocardial infarction (AMI) death of cardiac tissue due to lack of oxygen

adrenergic agonist a drug that stimulates adrenergic receptors, resulting in sympathetic nervous system stimulation

anaphylaxis systemic and overwhelming immune response to an antigen

angina discomfort in the front of the chest, neck, shoulders, jaw, or arms that is precipitated by physical exertion and is relieved by rest or sublingual nitrates

anticholinergic having the effect of inhibiting the cholinergic receptors, which then inhibits the parasympathetic nervous system

asystole a state of cardiac standstill; complete cessation of electrical activity of the heart

atrial fibrillation with rapid ventricular response a dysrhythmia that involves rapid electrical stimulation, causing the atria and ventricles to contract rapidly

calcium channel blocker a classification of drugs that prevent calcium from entering cells by binding to long-acting voltage-gated calcium channels in the heart, smooth muscle, and pancreas

cardiac output the product of the heart rate and stroke volume, or the amount of blood ejected with each heartbeat

cardiogenic shock shock caused by cardiac damage (pump failure)

defibrillation administration of electrical shock to a person experiencing a life-threatening cardiac dysrhythmia in an effort to restore normal sinus rhythm

dysrhythmia an irregular heart rhythm

hypovolemic shock decreased tissue perfusion caused by decreased circulating blood volume

infarction cell death due to lack of oxygen

inotropic agent a drug that causes the heart to contract with more force

ischemia deficient supply of blood to tissues, which can cause injury

nitrate a classification of drugs that cause vasodilation of blood vessels by imparting nitric oxide, which relaxes smooth muscles

opioid agonist a drug that stimulates the opioid receptors and decreases pain sensations

oxygen saturation measure of how much hemoglobin is bound to oxygen in the bloodstream

pulmonary edema excessive fluid in the lungs

pulseless electrical activity a life-threatening dysrhythmia in which the electrical system conducts impulses but the cardiac myocytes do not respond

pulseless ventricular tachycardia a life-threatening dysrhythmia in which the ventricles contract so rapidly that a pulse cannot be detected

shock decreased tissue perfusion to the point of hypoxia, which causes cells to undergo anaerobic metabolism; if not reversed, will lead to cell and tissue death

supraventricular tachycardia rapid heart rate that originates above the ventricles

symptomatic bradycardia heart rate less than 60 beats/min that causes the individual to have symptoms such as dizziness, lightheadedness, or fainting

systemic vascular resistance resistance to blood flow by the blood vessels

ventricular fibrillation a life-threatening dysrhythmia originating in the ventricles in which the ventricles are not coordinated in their contraction, leading to minimal cardiac output

ventricular tachycardia a dysrhythmia that originates from the ventricles and causes them to contract rapidly

Review Questions

1. The nurse is caring for a client receiving morphine 4 mg IV every 15 minutes for chest pain. Which assessment finding is of most concern to the nurse?

a. Heart rate 68 beats/min
b. Respiratory rate 8 breaths/min
c. Blood pressure 118/68 mm Hg
d. Oxygen saturation 95% on room air

2. The nurse has administered sublingual nitroglycerin to a client with chest pain. Which assessment finding does the nurse anticipate for this client?
a. An increase in respiratory rate
b. An increase in heart rate
c. A decrease in blood pressure
d. A decrease in oxygen saturation

3. At what rate should the nurse administer adenosine 6 mg IV to a client with supraventricular tachycardia?
a. Over 1–2 seconds
b. Over 1 minute
c. Over 5–10 minutes
d. Slowly over 1–2 hours

4. Which question should the nurse ask a client before administering nitroglycerin for chest pain?
a. Do you have lupus erythematosus?
b. Do you have a history of asthma?
c. Do you take any medications for erectile dysfunction?
d. Do you have Wolff–Parkinson–White syndrome?

5. The nurse in the emergency department is caring for a client who reports chest pain that is relieved at rest. Which diagnosis should the nurse anticipate?
a. Stable angina
b. Unstable angina
c. Myocardial infarction
d. Ventricular dysrhythmia

6. The health care provider has ordered diltiazem IV bolus 0.25 mg/kg for a client with atrial fibrillation with rapid ventricular response. The client weighs 176 lb (80 kg). What is the correct dose of diltiazem for the nurse to administer?
a. 15 mg
b. 20 mg
c. 25 mg
d. 30 mg

7. Which therapeutic response would the nurse anticipate when administering epinephrine to a client in anaphylaxis?
a. Bronchodilation
b. Bradycardia
c. Hypotension
d. Hypokalemia

8. Which adverse effect should the nurse monitor for in the client receiving dopamine by peripheral IV infusion?
a. Dizziness
b. Skin sloughing at the IV site
c. Electrolyte abnormalities
d. Facial flushing

9. The nurse in the cardiology clinic is caring for a client taking an antidysrhythmic medication for ventricular

dysrhythmia who develops a positive antinuclear antibody test. Which antidysrhythmic medication does the nurse anticipate this client is taking?

a. Amiodarone
b. Diltiazem
c. Lidocaine
d. Procainamide

10. What is the preferred route for administering epinephrine to a client with anaphylaxis who is in sinus tachycardia?

a. Intramuscular
b. Intravenous
c. Sublingual
d. Inhalation

CHAPTER 23
Introduction to the Respiratory System

FIGURE 23.1 The lungs are the core of the respiratory system, which moves oxygen into the body and waste gases out. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The respiratory system allows the body to breathe, talk, and smell. The respiratory system is primarily responsible for bringing oxygen into the body and is a major pathway to remove carbon dioxide and other waste gases. Adequate functioning of the respiratory system depends on having the nervous, cardiovascular, and musculoskeletal systems working properly as well. This will be discussed later in the chapter.

This chapter is separated into three sections: the upper respiratory system, the lower respiratory system (see Figure 23.2), and the system of oxygenation and gas exchange. This chapter will review both the upper and lower respiratory systems and will briefly discuss common conditions that affect the respiratory tract, oxygenation, and gas exchange (Cleveland Clinic, 2023).

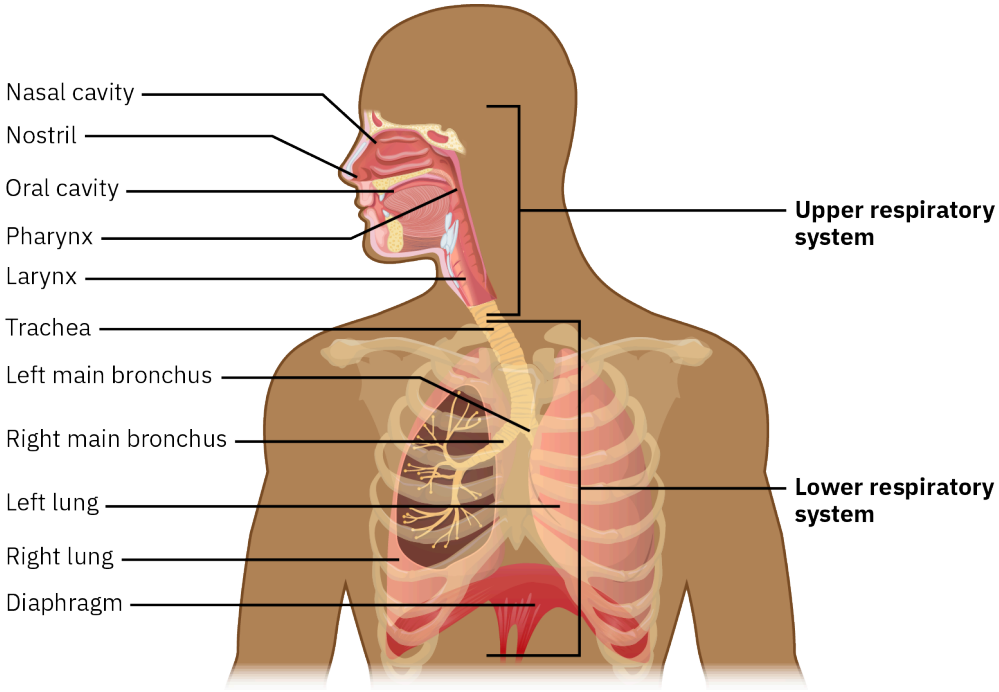


FIGURE 23.2 The respiratory system is divided into the upper respiratory system and lower respiratory system. (credit: modification of work from *Anatomy and Physiology 2e.* attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

23.1 Introduction to the Upper Respiratory System

By the end of this section, you should be able to:

- 23.1.1 Describe the major structures of the upper respiratory system and their function.
- 23.1.2 Discuss the common conditions that affect the upper respiratory system.

The upper respiratory system, shown in Figure 23.3, contains structures that allow us to breathe and speak, warm and clean the air we inhale, and trap foreign particles before air travels down to the lungs (Visible Body, 2023).

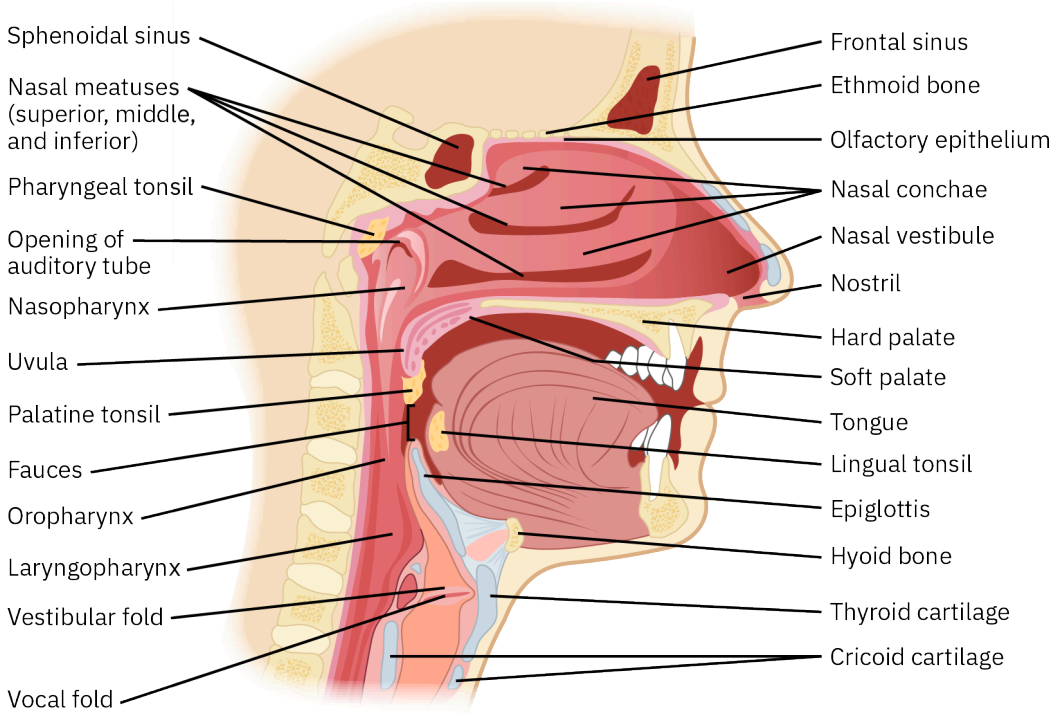


FIGURE 23.3 The upper respiratory system contains structures that help us breathe and speak. (credit: modification of work from *Anatomy and Physiology 2e.* attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Upper Respiratory System and Function

The upper respiratory tract consists of these structures (Cleveland Clinic, 2023):

- *Nose:* This is the entrance to the respiratory tract. It contains a small patch of tissue that is home to **olfactory** sensory neurons. These neurons allow for recognition of scents. The nose contains mucus and cilia. The mucus traps dirt and particles, and then the cilia move those particles out of the nose. The mucous membranes within the nose help to clean the inhaled air as well as moisten and warm it.
- *Nasal cavity:* This is a space inside the nose that is divided into two nasal passages. These passages are lined with respiratory mucosa to clean, moisten, and warm the inspired air.
- ***Sinus cavities**:* These are four air-filled, interconnected cavities located between the eyes and nose that produce and circulate mucus. They are typically empty except for a thin layer of mucus. The sinuses drain into the nose. They are commonly referred to as paranasal cavities.
- *Mouth:* This is an opening through which food and air enter the body. Although air can enter through the mouth, that air is not filtered as it is when entering the nose.
- *Throat (pharynx):* This carries air, food, and fluid down from the nose and mouth.
- *Voice box (larynx):* This protects the lower respiratory tract from food being aspirated into the trachea while breathing; it also contains the vocal cords.

Air is inhaled through the nose, where it is warmed and moistened by the vascular mucosa, and foreign material is filtered out by the mucus and hairs. This prevents foreign material from entering the lung tissue. Air can be inhaled through the mouth, but it is not warmed, moistened, or filtered properly before it travels through the upper and lower respiratory systems. Air from the nose then passes through the sinuses and is further filtered by the respiratory mucosa. The respiratory mucosa consists of the columnar epithelium, which includes the goblet cells and cilia. The mucus captures any foreign particles not cleared via the nasal passages, and the cilia sweep the mucus up and out of the respiratory tract. Air then continues through the pharynx and the larynx and into the trachea.

Upper Respiratory Conditions

Upper respiratory conditions usually involve an inflammatory response that can affect the mucosal layer of the airways and can lead to various health conditions. Some of the most common upper respiratory conditions are rhinitis, sinusitis, pharyngitis, and laryngitis. Each of these conditions can impact the ability of the airway to transport air to and from the lungs. Breathing difficulties and other respiratory symptoms can result from any of these conditions.

Rhinitis

Rhinitis is inflammation and swelling of the mucous membranes in the nose. It can be caused by a variety of factors including allergens such as pollen and animal dander, smoke, temperature, viral infection, and certain drugs. The inflammatory response that is triggered by these irritants causes the mucous membranes of the nose and pharynx to swell and increase secretion production. The increased production of secretions that drain down the throat can cause irritation and coughing. Common symptoms of rhinitis include:

- Stuffy and runny nose (with clear drainage)
- Sneezing
- Itchy nose, throat, and eyes
- Sore throat and coughing

Histamine is the substance in the body that produces many of these symptoms, but it is also involved in the immune response. Therefore, it is also a causative factor in the signs and symptoms of viral rhinitis.

Rhinitis can be acute, chronic, or year-round. Acute rhinitis is usually caused by viral illness and seasonal allergies. Rhinitis is considered chronic if it lasts longer than 4 weeks. Chronic rhinitis causes are often the same as those of acute rhinitis. Year-round rhinitis is considered an allergic rhinitis and occurs in clients who have allergic reactions to trees, pollen, animal dander, and other allergens.

Prevention and avoidance of triggering factors are the ideal methods for managing rhinitis, but if symptoms persist, treatment with antihistamines, decongestants, and nasal sprays may also be used (Johns Hopkins Medicine, n.d.-b).

Sinusitis

Sinuses are air-filled pockets located near the nasal passage. Because they are hollow, sinuses help reduce the weight of the facial bones. They make mucus that cleans bacteria and other particles out of the air being breathed.

Sinusitis is an infection or inflammation of the lining of the sinuses. Sinusitis can be acute, chronic, or recurring.

Symptoms of sinusitis include:

- Headache
- Facial pain
- Runny nose that lasts longer than 7–10 days
- Cough and sore throat
- Swelling around the eyes

Sinusitis is treated with antibiotics, pain relievers, and nasal decongestants or drops. A referral to an allergist or immunologist may be needed for chronic or recurrent sinusitis (Johns Hopkins Medicine, n.d.-c).

Pharyngitis and Laryngitis

Pharyngitis is inflammation of the pharynx. It is more commonly known as a sore throat. A diagnosis of pharyngitis is nonspecific and does not convey the etiology of the illness. It is typically caused by viral or bacterial infections such as the common cold, influenza, or strep throat. Strep throat is an infection caused by the Streptococcus A group of bacteria. The first symptom of strep throat is often a sore throat. Noninfectious causes of pharyngitis include allergies and gastroesophageal reflux disease (GERD).

Symptoms of pharyngitis include:

- Sore, dry, or scratchy throat
- Pain when swallowing or speaking

Pharyngitis treatment is dependent on the cause and may require antibiotics, pain relievers, and increased fluids to treat the symptoms (Johns Hopkins Medicine, n.d.-a).

Laryngitis is inflammation of the larynx. It will typically resolve without treatment in about a week. Symptoms typically begin suddenly and include hoarseness, difficulty speaking, sore throat, and irritating cough (NHS Inform, 2023).

23.2 Introduction to the Lower Respiratory System

By the end of this section, you should be able to:

- 23.2.1 Describe the structure and function of the lower respiratory system.
- 23.2.2 Discuss common conditions that affect the lower respiratory system.

The lower respiratory system, shown in Figure 23.4, consists of several organs including the trachea, bronchi, bronchioles, and alveoli, which together make up the lungs.

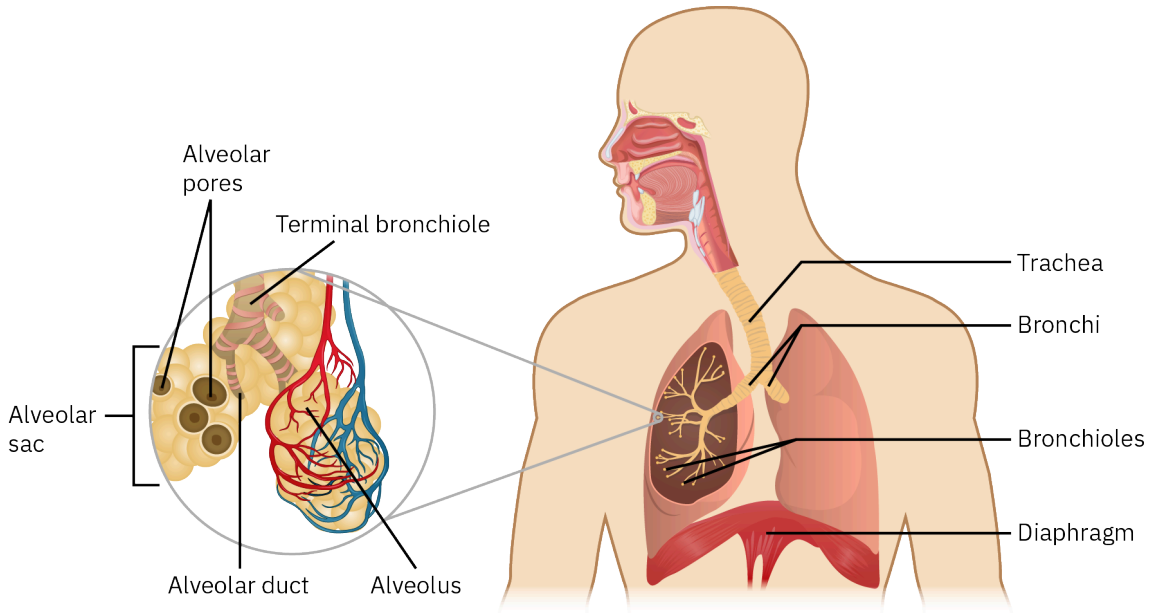


FIGURE 23.4 The lower respiratory system starts at the trachea and includes the lungs. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Lung Structure and Function

The lower respiratory tract consists of these structures:

- *Trachea (windpipe):* This carries inhaled air into the lungs.
- *Lungs:* These include the bronchi, bronchioles, and alveoli. Air enters the lungs for oxygen and carbon dioxide to be exchanged.
  - *Bronchi*: Major air passages that branch off from the trachea
  - *Bronchioles:* The smallest airways in the lungs

The lungs are air-filled organs on either side of the thorax. The right lung consists of three lobes, and the left lung consists of two lobes. Air travels from the larynx to the trachea, which is lined with smooth muscle and elastic tissue. Cartilage supports the airway and prevents collapse. The air then flows into branches called bronchi. The bronchi divide into smaller bronchioles until they become microscopic. At the end of the bronchioles are alveoli. Alveoli are microscopic air sacs where oxygen from the air is absorbed into the blood. Carbon dioxide travels from the blood to the alveoli so that it can be exhaled.

The function of the lungs can be assessed in a variety of ways. Assessing a client's respiratory rate can provide an insight into proper function. A normal respiratory rate for an adult should be 12–20 breaths per minute. **Pulmonary function tests (PFTs)** determine how well the lungs work. They measure how much air goes into and out of the lungs, how much air goes from the lungs to the blood, and how well the lungs work during exercise.

LINK TO LEARNING

Pulmonary Function Tests

Access multimedia content (https://openstax.org/books/pharmacology/pages/23-2-introduction-to-the-lower-respiratory-system)

This video from Columbus Community Hospital illustrates four pulmonary function tests that a client may need to undergo: spirometry, maximum voluntary ventilation (MVV), diffusion capacity testing, and lung volume measurements. It also shows examples of each test.

Lower Respiratory Conditions

Some of the most common lower respiratory conditions are asthma and chronic obstructive pulmonary disease

(COPD), which includes emphysema and chronic bronchitis.

Asthma

Asthma is a condition in which airways swell and become narrow. The airways may also produce extra mucus. The combination of these characteristics can make breathing difficult and cause coughing and wheezing (a whistling sound) when breathing out. Asthma often causes clients to feel short of breath. (Mayo Clinic, n.d.-a).

Asthma symptoms can vary from person to person and in severity. Clients may present with:

- Shortness of breath
- Chest tightness or pain
- Wheezing (inspiratory and expiratory)
- Sleep problems due to the previous symptoms

Symptoms can be worsened by respiratory viruses such as influenza. They also can be triggered by exercise, occupational exposure to chemicals or dust, and allergens such as pollen or mold. Asthma cannot be cured, but it can be treated and its symptoms controlled.

Diagnosis of asthma is made utilizing PFTs as described previously, typically spirometry, after a client has exhibited symptoms.

Preventing asthma attacks and long-term control are the main goals of treatment. Asthma is often treated with inhaled corticosteroid and inhaled bronchodilators. For treatment of acute asthma attacks, inhaled short-acting bronchodilators and anticholinergic agents such as ipratropium are often used (Mayo Clinic, n.d.-a).

LINK TO LEARNING

Breath Sounds

Access multimedia content (https://openstax.org/books/pharmacology/pages/23-2-introduction-to-the-lower-respiratory-system)

This video from EMTPrep provides examples of breath sounds, including the wheezing that one might hear in a client with asthma. Along with wheezing, it includes samples of bronchial breath sounds, crackles, diminished breath sounds, pleural rub, stridor, and vesicular breath sounds.

Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a group of conditions that cause the blockage of air flow and result in breathing issues. It includes emphysema and chronic bronchitis (discussed in the following sections). The main cause of COPD is tobacco smoke; other causes include air pollution, family history, and certain respiratory infections like pneumonia (Centers for Disease Control and Prevention, 2021).

Emphysema

Emphysema is characterized by shortness of breath. In clients with emphysema, the alveoli are damaged and do not work properly. Because of this damage, when the client exhales, old carbon dioxide–rich air becomes trapped and reduces room for fresh, oxygen-rich air. Emphysema is a progressive disorder. As time goes on, the inner walls of the alveoli become weak and rupture. This creates large air spaces in the lungs, which reduce the surface area of the lungs and how much oxygen reaches the bloodstream (Mayo Clinic, n.d.-b).

Symptoms of emphysema get progressively worse and include:

- Shortness of breath
- Wheezing
- Chronic cough

Many clients do not have symptoms for years, but eventually they may notice difficulty breathing during normal everyday activities.

Because smoking is the biggest risk factor for emphysema, smoking cessation is the most common preventative measure.

Emphysema is diagnosed through a client history, images such as x-rays, and pulmonary function tests.

Emphysema cannot be cured, but there are treatments that can decrease symptoms and slow the progression of the disease. Bronchodilators, inhaled corticosteroids, and, if needed, antibiotics are utilized. Many clients may need supplemental oxygen to ensure proper blood oxygen levels (Mayo Clinic, n.d.-b).

LINK TO LEARNING

Quitting Smoking

Access multimedia content (https://openstax.org/books/pharmacology/pages/23-2-introduction-to-the-lower-respiratory-system)
This video with Kristina Hamilton of the American Lung Association discusses the health benefits of smoking cessation. She discusses changes in health at certain time intervals when quitting and provides information on where to get additional information and support.

Chronic Bronchitis

Chronic bronchitis is a type of COPD characterized by inflammation and irritation of the bronchial tubes. This causes mucus buildup and difficulty moving air into and out of the lungs.

Chronic bronchitis is usually caused by exposure to irritants over a long period. In the United States, cigarette smoking is the main reason for this disorder (Johns Hopkins Medicine, 2019).

Symptoms of chronic bronchitis include:

- Frequent coughing
- Wheezing
- Shortness of breath
- Tightness in the chest

Although there is no cure for chronic bronchitis, it is possible to manage symptoms, slow disease progression, and improve quality of life. Nonpharmacologic treatments include lifestyle changes such as quitting smoking, increasing physical activity, and having a healthy diet.

Pharmacological therapy often includes bronchodilators, inhaled corticosteroids, and antibiotics if bacterial infection is suspected (Johns Hopkins Medicine, 2019).

23.3 Oxygenation and Gas Exchange

By the end of this section, you should be able to:

- 23.3.1 Describe the process of oxygenation.
- 23.3.2 Discuss the phases of gas exchange.

Two main functions of the lungs are oxygenation and gas exchange. Without these processes, the body would not get the oxygen that tissues and organs need and would not be able to expel waste gases from the body.

Oxygenation

Oxygenation is the process of supplying oxygen to body cells. When a person breathes in, oxygen diffuses and is picked up by the hemoglobin of the red blood cells. It is then transported and distributed to the organs and tissues of the body. All organs and tissues rely on oxygen to function properly.

The amount of oxygen bound to hemoglobin can be measured using oxygen saturation. This describes the percentage of hemoglobin currently bound to oxygen. Normal oxygen saturation is between 95% and 100% for a client breathing only room air.

When the tissues and organs lack oxygen, a condition called **hypoxemia** can result. Hypoxemia is lower-than-normal oxygen levels in the blood and often requires the client to receive concentrated oxygen. This condition can be fatal if not treated (Landry, 2022).

Gas Exchange

Gas exchange, shown in Figure 23.5, occurs when oxygen moves from the lungs to the bloodstream. For gas exchange to happen, the alveoli must be ventilated, gases must be diffused, and perfusion must take place. The pulmonary arteries bring venous blood from the right side of the heart to be oxygenated, and the gas exchange occurs in the pulmonary capillaries. The pulmonary veins then return the oxygenated blood to the left side of the heart, which pumps it out into the systemic circulation (Landry, 2022).

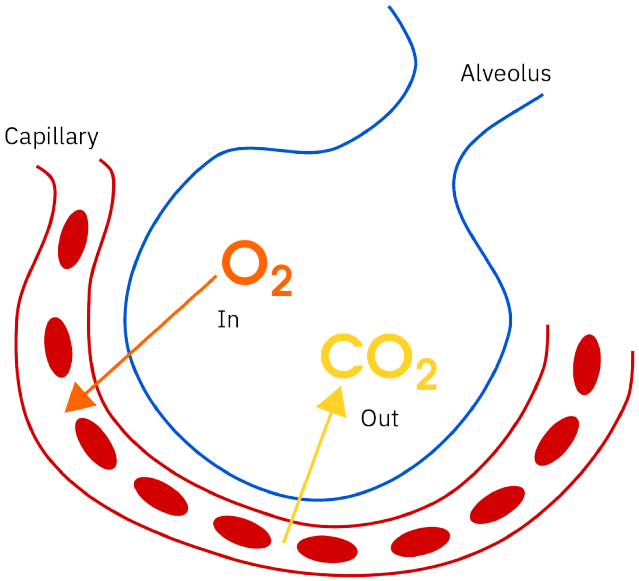


FIGURE 23.5 In the gas exchange process, oxygen moves into the bloodstream and carbon dioxide leaves it. (credit: modification of work "Gas exchange in the aveolus simple (blank with whitespace)" by Domdomegg/Wikimedia Commons, CC BY 4.0 International)

Ventilation

Ventilation is the process of moving air into and out of the lungs. It helps ensure that oxygen-rich air is brought into the lungs and carbon dioxide is expelled. The ventilation process also helps to maintain blood pH in the normal range by regulating the amount of carbon dioxide in the body.

Ventilation consists of inspiration and expiration. With inspiration, air flows into the body and travels through the respiratory system, down the airways, and into the alveoli. Upon normal expiration, the diaphragm and intercostal muscles relax, and air flows out of the alveoli and back through the respiratory system to the atmosphere (Landry, 2022).

Respiratory control is significantly influenced by chemical factors. Chemoreceptors sense changes in the levels of carbon dioxide, hydrogen ions, and oxygen in the blood. These receptors adjust the rate of ventilation in response to the amount of carbon dioxide in the blood. When carbon dioxide levels are too high, the respiratory rate increases to "blow off" the excess carbon dioxide. This, in turn, raises the pH level of blood because carbon dioxide is acidic. On the other hand, if carbon dioxide levels are too low, the respiratory rate will decrease to "hold on to" the carbon dioxide, thereby lowering the pH level (Landry, 2022).

Diffusion

Diffusion is the spontaneous movement of gases between the alveoli and capillaries in the lungs. This process does not require any use of energy or effort by the body. Diffusion of oxygen and carbon dioxide depends on the concentration or partial pressure of gases. The movement of gases always occurs from a high-pressure area to a low-pressure area. Diffusion can also be affected by the thickness of respiratory membranes and the thickness of the alveolar membrane (Dezube, 2023).

Perfusion

Perfusion is the process of blood flowing to tissues and organs, which is crucial for delivering oxygen and nutrients and removing waste products. Blood carries needed oxygen throughout the body, where it is used for various metabolic processes (Dezube, 2023).

In the lungs, perfusion takes place through the capillaries that surround the alveoli. This allows for the exchange of oxygen and carbon dioxide between the air in the lungs and the blood in the capillaries (Landry, 2022).

Perfusion can be affected by poor circulation, which reduces the amount of oxygen that is transported to the tissues and organs. Other factors that can affect perfusion are low circulating volume, the pumping ability of the heart, and low blood pressure (Dezube, 2023).

Chapter Summary

This chapter focused on the structures and functions of the respiratory system. The upper and lower respiratory systems were discussed. The upper respiratory system consists of the nose, nasal cavity, mouth, pharynx, and larynx. The upper respiratory system brings air into the body and warms that air before it enters the lungs. The lower respiratory system consists of the trachea and the lungs, which include the bronchi and bronchioles. The lungs are where gas exchange takes place to provide the body with oxygen and expel carbon dioxide.

Common disorders of the upper and lower respiratory system were discussed. Upper respiratory disorders include pharyngitis (sore throat), rhinitis, and sinusitis. Disorders of the lower respiratory system include asthma and the chronic obstructive pulmonary diseases emphysema and chronic bronchitis.

The process of gas exchange, oxygenation, ventilation, perfusion, and diffusion were briefly discussed. Gas exchange is when oxygen moves from the lungs into the bloodstream. Oxygenation is the process of supplying oxygen to the body's cells. Ventilation is the process of moving air into and out of the lungs, and diffusion is the spontaneous exchange of gases between the alveoli and capillaries in the lungs. Perfusion is blood flow to tissues and organs, which can also be affected by circulation.

Key Terms

asthma condition in which airways narrow and swell, causing wheezing and difficulty breathing
chronic bronchitis long-term inflammation of the bronchi, causing severe coughing spells
chronic obstructive pulmonary disease (COPD) a group of diseases that cause airflow blockage and breathing problems; includes emphysema and chronic bronchitis; also known as chronic obstructive pulmonary disorder
diffusion spontaneous exchange of gases between the alveoli, capillaries, and lungs
emphysema gradual damage of alveoli that causes shortness of breath
gas exchange when oxygen moves from the lungs into the bloodstream
histamine compound released by cells in response to allergy or inflammatory reactions
hypoxemia lack of oxygen in the tissues and organs
laryngitis inflammation of the larynx
olfactory relating to the sense of smell
oxygenation process that involves the absorption of oxygen throughout the body
perfusion blood flow to tissues and organs
pharyngitis inflammation of the pharynx; also known as a sore throat
pulmonary function tests (PFTs) noninvasive tests that show how well the lungs are working
rhinitis inflammation and swelling of mucous membranes in the nose
sinus cavities four air-filled, interconnected cavities located between the eyes and nose; produce and circulate mucus
sinusitis infection of the lining of the sinuses
ventilation process of moving air into and out of the lungs

Review Questions

1. A client presents to the clinic with a report of itchy eyes, runny nose, and sneezing. Which diagnosis should the nurse anticipate the provider will make for this client?
   a. Laryngitis
   b. Rhinitis
   c. Asthma
   d. Bronchitis

2. What assessment finding would the nurse anticipate in the client with a diagnosis of asthma?
   a. Inspiratory and expiratory wheezing
   b. Itchy, watery eyes
   c. Clear breath sounds
   d. Cyanosis of the nail beds

3. A 60-year-old client with a 35-year history of smoking two packs of cigarettes a day reports a chronic cough and thick sputum. Based on these assessment findings, the nurse suspects the client has which condition?

a. Emphysema
b. Asthma
c. Sinusitis
d. Chronic bronchitis

4. Which instruction should the nurse give to a client with allergic rhinitis to decrease symptoms?
a. "Keep a log of when symptoms occur so that triggers can be identified."
b. "Call your provider for antibiotics when symptoms occur."
c. "A nasal decongestant will not work for this condition."
d. "Stay away from people with bacterial respiratory infections."

5. The nurse is teaching a client with a respiratory disorder that they may have no symptoms initially but will gradually experience shortness of breath with normal day-to-day activities. Which condition is the nurse describing?
a. Bronchitis
b. Pharyngitis
c. Sinusitis
d. Emphysema

6. When providing discharge instructions to a client with COPD, which information should the nurse include?
a. "You may be more susceptible to infections."
b. "Your disease will be cured with the use of medications."
c. "You will need less oxygen over time."
d. "You should not exercise because it will aggravate your condition."

7. The nurse is caring for a client with emphysema. Which assessment allows the nurse to monitor the amount of oxygen bound to hemoglobin?
a. Respiratory rate
b. Oxygen saturation
c. Hemoglobin level
d. Breath sounds

8. A client at a health fair asks the nurse how they can reduce their risk of COPD. What lifestyle change can the nurse recommend?
a. Quit smoking
b. Reduce physical activity
c. Avoid vaccines
d. Decrease fluid intake

9. A client has been diagnosed with COPD and asks why they should quit smoking because the damage has already been done. What is an appropriate response by the nurse?
a. "You are right. Quitting now will not do anything to help you."
b. "Smoking cessation can prevent further damage and may help heal some lung tissue."
c. "You cannot take some of your medications while smoking."
d. "Quitting smoking will cure the disease."

10. A client with sinusitis reports facial discomfort and pressure. What can the nurse recommend to the client to help reduce these symptoms?
a. Pneumococcal vaccination
b. Cough drops
c. Pain reducers
d. Bronchodilators

CHAPTER 24
Upper Respiratory Disorder Drugs

FIGURE 24.1 The lungs are the core of the respiratory system, which moves oxygen into the body and waste gases out. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION This chapter will discuss common upper respiratory drugs. These drugs include antihistamines, decongestants**,** antitussives, expectorants, and mucolytics. These drugs are used to treat conditions such as allergies, colds, and cough. Indications for use and common adverse reactions will be explored. Also discussed will be nursing implications and client education for each drug.

24.1 Antihistamines and Decongestants

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 24.1.1 Identify the characteristics of antihistamine and decongestant drugs used to treat respiratory disorders.
- 24.1.2 Explain the indications, actions, adverse reactions, and interactions of antihistamine and decongestant drugs used to treat respiratory disorders.
- 24.1.3 Describe nursing implications of antihistamine and decongestant drugs used to treat respiratory disorders.
- 24.1.4 Explain the client education related to antihistamine and decongestant drugs used to treat respiratory disorders.

Antihistamines

Histamines are chemicals in the immune system. Histamines are released by the body as part of the immune

response to a foreign substance such as an allergen or pathogen. Histamine receptors are activated, and reactions occur. H1 receptors are found in smooth muscle cells, endothelial cells, and nerve endings. Activation of these receptors leads to various responses, including smooth muscle contraction, increased vascular permeability, itching, and sensory nerve stimulation. These receptors are involved in allergic reactions as well as regulating sleep–wake cycles and maintaining blood pressure. H2 receptors are mostly located in the stomach parietal cells, regulating gastric acid secretion. When these receptors are blocked, allergy symptoms can be reduced and stomach acid can be controlled.

Once the immune system detects an allergen, a sequence of events is triggered to safeguard the body. Chemical messages are dispatched to mast cells and basophils in various body parts, signaling them to release histamines (see Figure 24.2). These histamines then augment blood circulation in the vicinity of the allergen, which leads to inflammation. To illustrate, if the nose is impacted, histamines stimulate the mucous membranes to produce additional mucus, resulting in nasal congestion, sneezing, and runny nose. These symptoms can typically be relieved using antihistamines (Fowler, 2022).

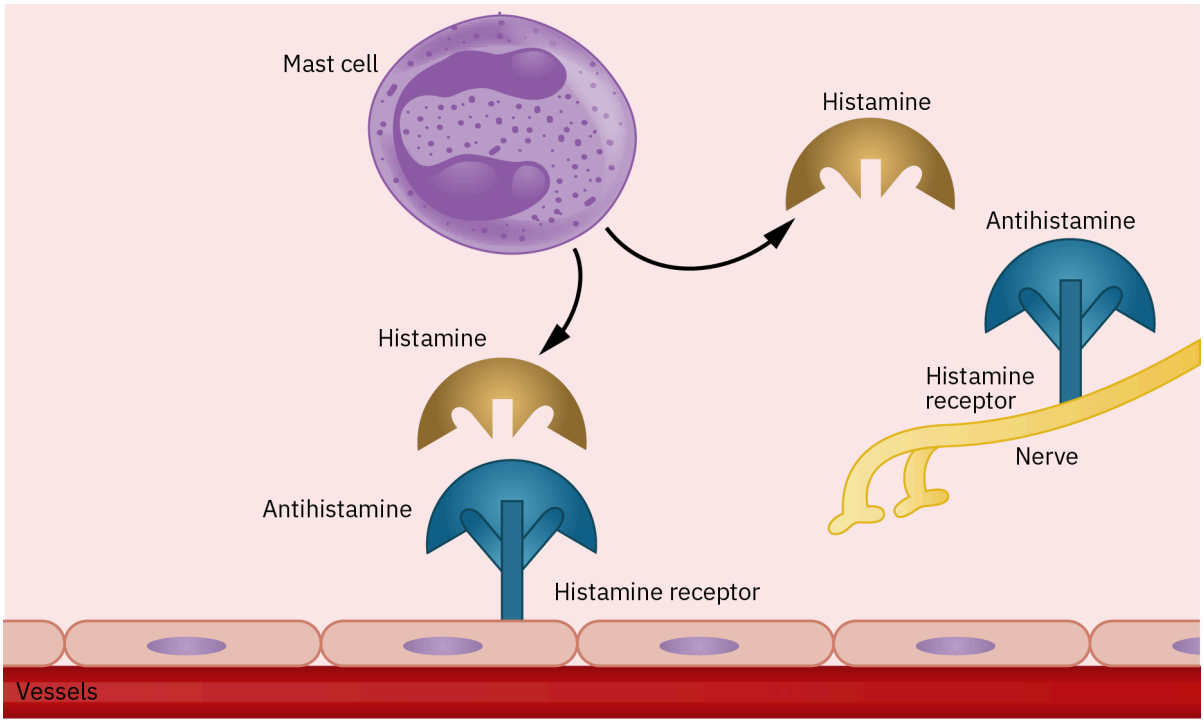


FIGURE 24.2 Antihistamines work by blocking the action of histamine. (credit: modification of work "Antihistamine" by Phn003 at English Wikibooks/Wikimedia Commons, Public Domain)

In addition to **antihistamines**, **decongestants** are another class of drugs that are commonly used for short-term relief of nasal congestion, or stuffy nose. A variety of disease processes can cause congestion, including colds, influenza, and allergies. Decongestants come in a wide array of forms including nasal sprays, drops, inhalers, and oral pills. Decongestants work by narrowing blood vessels and decreasing swelling and inflammation, which allows for easier breathing.

Antihistamines play a role in managing allergic reactions and mitigating the symptoms caused by histamine release in the body. The main method of achieving this is by competitively blocking or reducing the effects of histamine on target cellular receptors. Essentially, antihistamines obstruct the receptors in the brain that would typically respond to histamine (Johnson and Johnson, 2023). All three generations of antihistamines are beneficial for allergy relief, anti-inflammatory effects, respiratory symptoms relief, itch relief, and sleep. This chapter will focus on antihistamines as they relate to the respiratory system.

First-Generation Antihistamines

Antihistamines belonging to the first generation are extensively accessible and frequently used for managing allergy and cold symptoms. They were among the earliest antihistamines developed. These medications impact the histamine receptors present in the brain and spinal cord. Because they can penetrate the blood–brain barrier, they

may lead to drowsiness as a side effect. These antihistamines usually take around 30–60 minutes to take effect and provide relief that lasts for 4–6 hours. A commonly used first-generation antihistamine is diphenhydramine (Sicari & Zabbo, 2023). Table 24.1 lists common first-generation antihistamines and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Diphenhydramine (Benadryl)	25–50 mg orally every 4–6 hours; not to exceed 12 capsules in 24 hours.
Chlorpheniramine (Chlor-Trimeton)	4 mg orally every 4–6 hours, not to exceed 6 tablets in 24 hours.
Brompheniramine (Dimetapp)	20 mL orally every 4 hours not to exceed 6 doses in 24 hours; measure only with dosage cup provided.

TABLE 24.1 **Drug Emphasis Table: First-Generation Antihistamines** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

First-generation antihistamines can cause drowsiness, dizziness, confusion, and urinary retention. Clients with a history of urinary retention or prostatic hyperplasia should use first-generation antihistamines cautiously. First-generation antihistamines should be avoided in older adults because they can increase the risk of dementia.

Table 24.2 is a drug prototype table for first-generation antihistamines featuring diphenhydramine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antihistamine **Mechanism of Action** Antagonizes histamine H1 receptor sites, thereby hindering the actions triggered by histamine	**Drug Dosage** 25–50 mg orally every 4–6 hours, not to exceed 12 capsules in 24 hours.
Indications Rhinitis Allergy symptoms Motion sickness Nighttime sleep aid **Therapeutic Effects** Reduces nasal congestion, sneezing, and coughing Causes drowsiness that can aid in sleeping Prevents motion-related nausea	**Drug Interactions** Other central nervous system (CNS) depressants MAO inhibitors **Food Interactions** Alcohol
Adverse Effects Drowsiness Dizziness Confusion Hypotension Dry mouth Urinary retention	**Contraindications** Hypersensitivity Caution: Angle-closure glaucoma Stenosing peptic ulcer Prostatic hyperplasia

TABLE 24.2 **Drug Prototype Table: Diphenhydramine** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Antihistamines and Older Clients

First-generation antihistamines should be avoided in older clients. Their highly anticholinergic properties can increase the risk of dementia, and clearance of the drug is reduced in clients of advanced age.

Second-Generation Antihistamines

The mechanism of action and side effects of second-generation antihistamines are distinct from those of first-generation antihistamines. Unlike first-generation antihistamines, which block both histaminic and **muscarinic** receptors and can penetrate the blood–brain barrier, second-generation antihistamines primarily target histamine receptors and do not cross the blood–brain barrier, which therefore diminishes the likelihood of central nervous system–related adverse effects. This distinction leads to a significantly reduced occurrence of first-generation side effects, especially drowsiness, in second-generation antihistamines (Naqvi & Gerriets, 2023).

Cetirizine

Initially, cetirizine was a prescription-only second-generation antihistamine, but it was subsequently approved as an over-the-counter (OTC) medication and is now readily accessible. It is a potent treatment for allergic rhinitis and effectively alleviates symptoms such as sneezing, watery eyes, and rhinorrhea. Additionally, cetirizine has been identified as a primary therapeutic option for individuals with chronic **urticaria**. The effectiveness of cetirizine and its minimal side effects make it a very popular option for clients (Naqvi & Gerriets, 2023).

Levocetirizine

Levocetirizine is another second-generation antihistamine that effectively treats allergic rhinitis and its associated symptoms. Like other second-generation antihistamines, including cetirizine, it does not penetrate the blood–brain barrier, resulting in a lower occurrence of side effects when compared to first-generation antihistamines (DailyMed, *Levocetirizine,* 2011).

Loratadine

Loratadine is also a second-generation antihistamine and is available over the counter. It is effective in pruritus, allergic rhinitis, and sneezing related to seasonal allergies. Loratadine should not be used if a client is pregnant or breastfeeding until they have consulted with their health care provider (MedlinePlus, 2022).

Table 24.3 lists common second-generation antihistamines and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Cetirizine (Zyrtec)	One 10 mg tablet orally once daily. Do not take more than one 10 mg tablet daily. A 5 mg product may be used for less severe symptoms and for older clients.
Levocetirizine (Xyzal)	One 5 mg tablet orally once daily in the evening. Do not take more than one 5 mg tablet in 24 hours. One-half of a tablet (2.5 mg) once daily may be appropriate for less severe symptoms.
Loratadine (Claritin)	One 10 mg tablet orally daily, not to exceed more than 1 tablet in a 24-hour period. Also available in chewable and dissolving tablets and oral solution.

TABLE 24.3 **Drug Emphasis Table: Second-Generation Antihistamines** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Second-generation antihistamines have a lower incidence of adverse effects than first generation, but they can still cause drowsiness, sedation, dry mouth, and insomnia. Clients with hepatic or renal impairment should use second-generation antihistamines cautiously, and those with hypersensitivity to the medication should avoid use.

Table 24.4 is a drug prototype table for second-generation antihistamines featuring loratadine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antihistamine, second generation **Mechanism of Action** Blocks effects of histamine at H1 receptor sites	**Drug Dosage** One 10 mg tablet orally daily, not to exceed more than 1 tablet in a 24-hour period. Also available in chewable and dissolving tablets and oral solution.
Indications Allergic rhinitis To relieve itching due to hives (urticaria) **Therapeutic Effects** Relieves runny nose, sneezing, and itchy watery eyes caused by allergies Relieves itching due to hives	**Drug Interactions** Ketoconazole Macrolide antibiotics (may increase loratadine level) **Food Interactions** Alcohol
Adverse Effects Headache Drowsiness Sedation Fatigue Insomnia Nervousness Dry mouth	**Contraindications** Hypersensitivity Caution: Hepatic or renal impairment

TABLE 24.4 **Drug Prototype Table: Loratadine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Third-Generation Antihistamines

The latest type of antihistamines, known as third-generation antihistamines, are among the newest antihistamines available. They were designed to effectively treat the same conditions as previous antihistamines but without the potential risk of cardiac toxicity that was observed in clients with metabolic issues. This new generation offers a safer alternative for such individuals, and as with the second generation, the likelihood of experiencing negative side effects is decreased. The reduced incidence of side effects is related to the inability of third-generation antihistamines to cross the blood–brain barrier and affect the central nervous system. Second- and third-generation antihistamines are favored compared to the first generation due to their effectiveness and safety profile (Ricciardi et al., 2019).

Fexofenadine is a recently developed third-generation antihistamine (Sakur et al., 2022) for managing allergic rhinitis and chronic urticaria, and it has been approved for use by individuals of all ages, including children. Compared to other antihistamines, fexofenadine has demonstrated greater efficacy in relieving eye and nasal congestion symptoms. Clients who are pregnant or breastfeeding should seek advice from their health care provider before taking this medication because it can decrease breast milk production. It is not usually prescribed during pregnancy. Fexofenadine can cause headaches and dizziness (NHS, 2021).

Desloratadine, an active metabolite of the second-generation antihistamine loratadine, is a highly selective medication that is considerably more powerful than loratadine in treating allergy symptoms and urticaria (DailyMed, *Loratadine*, 2009).

Table 24.5 lists common third-generation antihistamines and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Fexofenadine (Allegra)	*12-hour tablet:* 60 mg orally with water every 12 hours. No more than 2 tablets in 24 hours. *24-hour tablet:* 180 mg orally with water once daily. No more than 1 tablet in 24 hours.
Desloratadine (Clarinex)	5 mg tablet orally once daily; if using the syrup, 2 teaspoonfuls (5 mg in 10 mL) orally once daily.

TABLE 24.5 **Drug Emphasis Table: Third-Generation Antihistamines** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Third-generation antihistamines, much like second-generation antihistamines, have a lower incidence of adverse

effects than first generation, but they can still cause fatigue, dizziness, nausea, and insomnia. Third-generation antihistamines should be used cautiously in clients with impaired renal function, and those with hypersensitivity should avoid using them.

Table 24.6 is a drug prototype table for third-generation antihistamines featuring fexofenadine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antihistamine, third generation **Mechanism of Action** Inhibits peripheral H1 receptors	**Drug Dosage** *12-hour tablet:* 60 mg orally with water every 12 hours. No more than 2 tablets in 24 hours. *24-hour tablet:* 180 mg orally with water once daily. No more than 1 tablet in 24 hours.
Indications Seasonal allergies Chronic idiopathic urticaria **Therapeutic Effects** Relief of allergy symptoms such as runny nose and itchy, watery eyes Relief of itching from chronic urticaria	**Drug Interactions** Aluminum or magnesium antacids Erythromycin Ketoconazole Rifampin **Food Interactions** Fruit juices (may decrease drug effects) Alcohol
Adverse Effects Fatigue Fever Headache Dizziness Insomnia Otitis media Rhinorrhea Nausea Abdominal pain	**Contraindications** Hypersensitivity Caution: Impaired renal function

TABLE 24.6 **Drug Prototype Table: Fexofenadine** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Antihistamines

Ingesting antihistamines in doses exceeding the recommended amount, particularly diphenhydramine, may result in severe heart complications, seizures, unconsciousness, or even fatality. Clients should avoid combining antihistamines with substances that are also sedating (sedatives, alcohol, etc.).

CLINICAL TIP

Antihistamine Education

When educating clients on the use of antihistamines, the nurse should tell them to call the health care provider if their symptoms last for more than 1 week, worsen, or are accompanied by other symptoms such as a headache that will not go away, a fever, or a rash. These may indicate a more serious medical condition.

SPECIAL CONSIDERATIONS

Antihistamines

Antihistamines can cause marked drowsiness and should be avoided when driving or operating machinery.

Alcohol and other CNS depressants can increase drowsiness and should be avoided when taking antihistamines.

Clients also should tell their health care provider if they are pregnant, plan to become pregnant, or are breastfeeding.

(Source: MedlinePlus, 2022)

Decongestants

Decongestants refer to medications that offer temporary relief for a blocked nose or nasal congestion. They can alleviate the stuffiness commonly associated with allergies, sinusitis, colds, and the flu. These medications function by diminishing the inflammation of the blood vessels in the nose, resulting in opening of the air passage. Two types of decongestants are systemic decongestants and topical, or nasal, decongestants (Corren, 2017).

Nasal Decongestants

Nasal decongestants are typically available as drops or sprays applied directly to the nasal passage. These remedies are regarded as topical agents and do not have any widespread impacts on the body. They are usually favored over oral drugs since they deliver prompt relief from nasal congestion. Nasal decongestants should be used for 3 days or less, as **rebound congestion** can occur. Rebound congestion is worsened congestion after the medication wears off.

Oxymetazoline

Oxymetazoline is a nasal spray that helps alleviate nasal congestion induced by allergies and colds. It may also relieve sinus pressure and congestion. Despite its convenience, this medication should be used only briefly. Overuse, beyond 3 days, can result in rebound congestion, where inflammation of the nasal mucosa occurs due to excessive use of nasal drops or sprays. Oxymetazoline is considered a local decongestant because it acts on the nasal tissue by narrowing the blood vessels and opening the air passages to allow for ease of breathing, producing no systemic effects. The lack of systemic effects can be beneficial to clients with hypertension or other cardiac disorders.

Adverse Effects and Contraindications

Rebound congestion can occur if used for more than 3 days. Some clients may experience temporary discomfort such as burning when used. Those who are hypersensitive should avoid their use.

Table 24.7 is a drug prototype table for the nasal decongestant oxymetazoline. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nasal decongestant **Mechanism of Action** Causes vasoconstriction of the nasal mucosa to alleviate nasal congestion	**Drug Dosage** 2–3 sprays in each nostril not more often than every 10–12 hours. Do not exceed 2 doses in any 12-hour period. Do not use for longer than 3 days to avoid rebound congestion.
Indications Nasal congestion caused by common colds, allergies, and other respiratory conditions **Therapeutic Effects** Reduces nasal congestion	**Drug Interactions** Albuterol Bupropion **Food Interactions** Caffeine
Adverse Effects Temporary discomfort such as burning or stinging Rebound congestion (if used for more than 3 days)	**Contraindications** Hypersensitivity

TABLE 24.7 **Drug Prototype Table: Oxymetazoline** (source: https://dailymed.nlm.nih.gov/dailymed/)

Systemic Decongestants

Systemic decongestants act by causing vasoconstriction of the nasal mucosa, relieving nasal congestion. Unlike topical nasal decongestants, systemic decongestants can cause more side effects. Nervousness, heart palpitations, insomnia, and tachycardia can be seen. Systemic decongestants act on alpha-adrenergic receptors in the blood vessel walls and can cause an increase in blood pressure and affect the cardiovascular system. Clients with cardiac issues should use systemic decongestants with caution because they can also increase blood pressure.

Pseudoephedrine

Pseudoephedrine is a systemic decongestant used to relieve nasal congestion. Pseudoephedrine can be purchased over the counter; however, it is highly regulated due to the use of some components of the drug to make **methamphetamine**. The drug typically must be requested from the pharmacist, but specific regulations may vary by state (American Addiction Centers, 2023). Clients should avoid caffeine when taking this drug, and those with blood pressure issues should discuss use of this medication with their health care provider. Pseudoephedrine is often found in combination with other medications. Clients should check labels carefully to avoid taking too much of the same medication (MedlinePlus, 2018).

Phenylephrine

Phenylephrine is another common nasal decongestant. This drug is an alpha-adrenergic agonist. It can be administered via tablet, liquid, or dissolving strip. It works as other decongestants do by reducing the swelling of the blood vessels in the nose. As with pseudoephedrine, those with blood pressure issues should consult with their health care provider before taking this medication because it can cause an increase in blood pressure.

Table 24.8 lists common systemic decongestants and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Pseudoephedrine (Sudafed)	One 120 mg tablet orally every 12 hours; do not take more than 2 tablets in 24 hours. One 240 mg tablet orally every 24 hours; do not take more than 1 tablet in 24 hours. *Immediate release:* 30–60 mg orally every 4–6 hours; maximum dose: 240 mg/day.
Phenylephrine (Sudafed PE)	One 10 mg tablet orally every 4 hours; do not take more than 6 doses in 24 hours.

TABLE 24.8 **Drug Emphasis Table: Systemic Decongestants** (sources: https://dailymed.nlm.nih.gov/dailymed/; MedlinePlus, 2018)

Adverse Effects and Contraindications

Systemic decongestants can cause increased blood pressure as well as nervousness, dizziness, and sleeplessness. Those clients with a hypersensitivity should avoid their use, and clients with heart disease and high blood pressure should use the drugs with caution and under the guidance of their health care provider.

Table 24.9 is a drug prototype table for systemic decongestants featuring pseudoephedrine. It lists drug class,

mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Systemic nasal decongestant **Mechanism of Action** Acts directly on adrenergic receptors and produces vasoconstriction, which shrinks nasal mucosa	**Drug Dosage** One 120 mg tablet orally every 12 hours; do not take more than 2 tablets in 24 hours. One 240 mg tablet orally every 24 hours; do not take more than 1 tablet in 24 hours. *Immediate release:* 30–60 mg orally every 4–6 hours; maximum dose: 240 mg/day.
Indications Relief of nasal congestion caused by colds, flu, and allergies **Therapeutic Effects** Relief of nasal congestion	**Drug Interactions** Metoprolol Albuterol Metformin Guaifenesin **Monoamine oxidase inhibitors (MAOIs)** **Food Interactions** Caffeine Alcohol
Adverse Effects Nervousness Dizziness Insomnia	**Contraindications** Hypersensitivity Caution: Heart disease High blood pressure Diabetes

TABLE 24.9 **Drug Prototype Table: Pseudoephedrine** (source: https://dailymed.nlm.nih.gov/dailymed/)

LINK TO LEARNING

Adrenergic Agonists

Access multimedia content (https://openstax.org/books/pharmacology/pages/24-1-antihistamines-and-decongestants)

This video discusses how decongestants work to alleviate nasal decongestion.

SAFETY ALERT

Phenylephrine vs. Pseudoephedrine

For clients with high blood pressure, phenylephrine should be used instead of pseudoephedrine. Phenylephrine has less impact on blood pressure than pseudoephedrine.

CLINICAL TIP

Decongestant Education

When educating clients on the use of decongestants, the nurse should tell them to call their health care provider if their symptoms last for more than 1 week, worsen, or are accompanied by other symptoms such as a headache that will not go away, a fever, or a rash. These may indicate a more serious medical condition.

SPECIAL CONSIDERATIONS

Decongestants

Decongestants and nasal drops should be used per the label instructions and not more to avoid rebound congestion.

Decongestants are not safe for children under age 6.

Clients should increase fluid intake when taking any cold medication, including decongestants.

(Source: MyHealth.Alberta.ca Network, 2022)

Nursing Implications

The nurse should do the following for clients who are taking antihistamines or decongestants:

- Prior to administering, assess the client's medical history, current drug list, and allergies for potential interactions and contraindications.
- Educate the client on adverse effects of antihistamines including drowsiness, dizziness, and dry mouth.
- Educate the client on adverse effects of decongestants including nervousness, dizziness, and rebound congestion (nasal sprays).
- Monitor vital signs for hypotension and respiratory depression (antihistamines) and hypertension and irregular heart rhythms (decongestants).
- Monitor urinary input and output for urinary retention.
- Initiate fall precautions for older clients due to the adverse effects of hypotension, dizziness, and drowsiness (antihistamines).
- Provide oral care and lozenges or saliva substitute for dry mouth (antihistamines).
- Instruct the client on administration technique for nasal decongestant spray.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antihistamine should:

- Check with their health care provider before taking if they have glaucoma, peptic ulcer disease, or urinary retention or are pregnant.
- Take antihistamines only as prescribed, not exceeding the recommended amount.
- Use sugarless candies or lozenges if dry mouth is experienced.

The client taking an antihistamine *should not:*

- Drive a car, operate machinery, or perform other tasks that require alertness when taking first-generation antihistamines due to their causing drowsiness and/or dizziness.
- Take more than one antihistamine at a time. Often OTC drugs contain a combination of drugs that may contain antihistamines.

The client taking a decongestant should:

- Take the drug as directed.
- Report any adverse effects or symptoms not relieved within 1 week.
- Be sure to take in fluids and maintain hydration.
- Use a humidifier to prevent drying of the nasal passages.
- Avoid exposure to triggers that may cause congestion.

The client taking a decongestant *should not:*

- Use nasal sprays for more than 3 days.

- Consume caffeine and alcohol while taking decongestants.
- Take any OTC drugs with this medication without consulting their health care provider.
- Take the drug within 2 hours of bedtime because it may cause restlessness and insomnia.

24.2 Antitussives

By the end of this section, you should be able to:

- 24.2.1 Identify the characteristics of antitussive drugs used to treat respiratory disorders.
- 24.2.2 Explain the indications, actions, adverse reactions, and interactions of antitussive drugs used to treat respiratory disorders.
- 24.2.3 Describe nursing implications of antitussive drugs used to treat respiratory disorders.
- 24.2.4 Explain the client education related to antitussive drugs used to treat respiratory disorders.

Opioid Antitussives

Antitussives are drugs that are used to treat nonproductive coughs. They are more commonly referred to as cough suppressants. Although their exact mechanism of action is unknown, it is thought that these medications inhibit the cough center in the brain or soothe nerve receptors around airways to reduce transmission of cough signals to the brain. Antitussives are not recommended for productive coughs where the client is coughing up mucus due to the infection risk that can result from the buildup of mucus in the respiratory system. Many antitussives are available over the counter, but there are a few that are prescription only (Sison, 2022).

Opioid antitussives are very effective and are thought to act centrally in the brain stem as well as on sensory nerve endings in the airways. The main concern with opioid antitussives is the potential for dependence, respiratory depression, and gastrointestinal issues such as constipation. Due to the opioid component, addiction is a concern, as is overdose of the drug.

Codeine/Guaifenesin

Codeine/guaifenesin is an opioid drug that is very effective as an antitussive, or cough suppressant. The drug works by suppressing the cough reflex through direct action on the cough center in the medulla. Because it contains codeine, which is an opioid, there is concern about adverse effects such as respiratory depression and dependence (MedlinePlus, 2023).

Adverse Effects and Contraindications

Opioid antitussives can cause drowsiness, dizziness, confusion, and hypotension. Dependence is also a concern due to the opioid portion. Those who are hypersensitive to them should avoid their use. Clients with angle-closure glaucoma, pyloric stenosis, peptic ulcer disease, and prostatic hyperplasia should also avoid opioid antitussives.

Table 24.10 is a drug prototype table for opioid antitussives featuring codeine/guaifenesin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Opioid antitussive **Mechanism of Action** Acts on the cough center in the medulla to suppress the cough reflex	**Drug Dosage** 20 mg orally every 4 hours as needed.
Indications Nonproductive cough, especially chronic cough **Therapeutic Effects** Reduces coughing episodes	**Drug Interactions** Other CNS depressants Benzodiazepines Bupropion Macrolide antibiotics Muscle relaxers Serotonergic drugs St. John's wort **Food Interactions** Alcohol
Adverse Effects Drowsiness Dizziness Confusion Hypotension Constipation Respiratory depression	**Contraindications** Hypersensitivity Caution: Angle-closure glaucoma Stenosing peptic ulcer Prostatic hyperplasia

TABLE 24.10 **Drug Prototype Table: Codeine/Guaifenesin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nonopioid Antitussives

Nonopioid antitussives are antitussives that do not contain an opioid component. Because of the lack of an opioid, there are no opioid-related side effects. These drugs work by numbing the throat and suppressing the cough. Drowsiness, dizziness, headache, and trouble sleeping are common side effects of these drugs.

Benzonatate

Benzonatate is a nonopioid antitussive that works by reducing the cough reflex in the airways and lungs. The drug comes as a capsule, taken orally. Clients should discuss with their health care provider any medications they are currently taking and inform the provider immediately if they experience rash, itching, or confusion because these are adverse effects (MedlinePlus, 2017).

Dextromethorphan

Dextromethorphan acts to suppress cough by acting on the cough center in the medulla. This drug is a common choice for relief of cough because it does not cause addiction and has little to no CNS depression. Clients should inform their health care provider if their cough lasts longer than 1 week or is accompanied by other symptoms such as fever or rash.

Table 24.11 lists common nonopioid antitussives and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Benzonatate (Tessalon)	One 100 mg or one 200 mg capsule orally 3 times daily as needed. Maximum dose: 600 mg/day.
Dextromethorphan (Robitussin)	15 mg orally every 4 hours as needed. Maximum dose: 120 mg/day.

TABLE 24.11 **Drug Emphasis Table: Nonopioid Antitussives** (source: https://dailymed.nlm.nih.gov/dailymed/; MedlinePlus, 2017)

Adverse Effects and Contraindications

Adverse effects of nonopioid antitussives include rash, itching, confusion, nausea, and constipation. Some clients

may also experience lightheadedness, dizziness, and drowsiness. Clients with a hypersensitivity to nonopioid antitussives should avoid their use, and they should be used with caution in clients who are sedated or must remain supine.

Table 24.12 is a drug prototype table for the nonopioid antitussives featuring dextromethorphan. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nonopioid antitussive **Mechanism of Action** Main action is not well known, but thought to act on the site in the brain stem that acts as the gate for the cough reflex	**Drug Dosage** 15 mg orally every 4 hours as needed. Maximum dose: 120 mg/day.
Indications Nonproductive coughs **Therapeutic Effects** Temporarily relieves cough caused by throat and bronchial irritation due to colds or allergies	**Drug Interactions** MAOIs **Food Interactions** Grapefruit juice
Adverse Effects Drowsiness Dizziness Confusion Nausea Vomiting	**Contraindications** Hypersensitivity Children under age 4 Caution: Clients who are sedated or must remain in a supine position (these clients may have an inability to clear their airway appropriately)

TABLE 24.12 **Drug Prototype Table: Dextromethorphan** (source: https://dailymed.nlm.nih.gov/dailymed/)

LINK TO LEARNING

Cough Reflex and Antitussives

Access multimedia content (https://openstax.org/books/pharmacology/pages/24-2-antitussives)
This video discusses the cough reflex and how antitussives work to suppress cough.

SAFETY ALERT

Antitussives and Older Adults

Opioid antitussive doses may need to be reduced in older adults. Older adults are more sensitive to opioids and more likely to have adverse reactions.

CLINICAL TIP

Antitussive Education

When educating clients on use of antitussives, the nurse should tell them to call their health care provider if their cough last for more than 1 week, worsens, or is accompanied by other symptoms such as a headache that will not go away, a fever, or a rash. These may indicate a more serious medical condition.

SPECIAL CONSIDERATIONS

Antitussives

Opioid antitussives can cause respiratory depression. Respirations should be monitored closely.

Antitussives can cause drowsiness, and clients should avoid driving until they know how the drug will affect them.

Antitussives should not be taken longer than recommended to prevent serious adverse effects.

(Source: Nurselabs, 2023)

Nursing Implications

The nurse should do the following for clients who are taking antitussives:

- Prior to administering, assess the client's medical history, current drug list, and allergies for potential interactions and contraindications.
- Prior to administering, assess the client's respiratory status for signs of respiratory distress that indicate additional evaluation and treatment is indicated.
- Assess and monitor the client's cough including type and frequency.
- Educate the client on adverse effects of antitussives including drowsiness, dizziness, constipation (opioid antitussives), and nausea and vomiting (nonopioid antitussives).
- For clients taking opioid antitussives, monitor vital signs for hypotension and respiratory depression before and after administration.
- For clients taking opioid antitussives, monitor for misuse or abuse.
- For clients taking opioid antitussives, the nurse should instruct the client on how to maintain healthy bowel habits to avoid constipation.
- Initiate fall precautions for older clients due to the adverse effects of hypotension, dizziness, and drowsiness (opioid antitussives).
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antitussive should:

- Take the medication as prescribed and should not exceed recommended doses.
- Report a cough that lasts longer than 1 week or is accompanied by other symptoms.
- Report symptoms of respiratory depression.
- Take measures to prevent constipation.
- Keep all antitussives out of the reach of children.
- Avoid irritants, such as smoking, that can cause more coughing.
- Increase fluid intake to help loosen secretions.

FDA BLACK BOX WARNING

Antitussives

Antitussives containing codeine have a high risk of addiction, abuse, and misuse.

24.3 Expectorants and Mucolytics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 24.3.1 Identify the characteristics of expectorant and mucolytic drugs used to treat respiratory disorders.
- 24.3.2 Explain the indications, actions, adverse reactions, and interactions of expectorant and mucolytic drugs used to treat respiratory disorders.
- 24.3.3 Describe nursing implications of expectorant and mucolytic drugs used to treat respiratory disorders.
- 24.3.4 Explain the client education related to expectorant and mucolytic drugs used to treat respiratory disorders.

Expectorants

Expectorants are a class of drugs that help to clear mucus from the airways when coughing. Expectorants can be stand-alone drugs or can be a part of combination cold and flu preparations. Expectorants do not suppress the cough like antitussives do, so they should only be used with productive coughs when it is necessary to loosen and clear mucus. Expectorants work by lubricating the airways, stimulating the cough reflex, and decreasing mucus viscosity so that it is easier to expel (Cleveland Clinic, 2021).

Guaifenesin

Guaifenesin is a common expectorant and is available over the counter without a prescription. It increases production of respiratory tract fluids to help liquefy mucus and make it easier to expel.

Adverse Effects and Contraindications

Guaifenesin does not cause many adverse effects, but dizziness, headache, nausea, and vomiting may occur.

Table 24.13 is a drug prototype table for expectorants featuring guaifenesin. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Expectorant **Mechanism of Action** Increases production of respiratory tract fluids to liquefy mucus	**Drug Dosage** 200 mg orally every 4 hours. *Extended-release tablets:* 600–1200 mg orally every 12 hours. Maximum dose: 2400 mg daily.
Indications Productive coughs where there is a need to clear the airway of mucus **Therapeutic Effects** Thinner mucus that is easy to cough up and expel	**Drug Interactions** Cimetidine Naltrexone **Food Interactions** No significant interactions
Adverse Effects Headache Dizziness Nausea Vomiting Urticaria	**Contraindications** Hypersensitivity Children under age 12 (extended-release preparations) Caution: Pregnancy

TABLE 24.13 **Drug Prototype Table: Guaifenesin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Mucolytics

Mucolytics also help clients to clear mucus from the airway. They differ from expectorants in that they are used to help high-risk respiratory clients cough up thick, tenacious mucus. Mucolytics directly break down the structure of mucus by breaking its protein bonds, helping to reduce the thickness and stickiness of mucus. Clients with

tracheostomies often benefit from mucolytics. Mucolytics are also sometimes used to clear the airway in preparation for a bronchoscopy.

Acetylcysteine

Acetylcysteine is used to help clients clear thick, tenacious mucus from the airways. It is often used in clients with pneumonia, bronchitis, **cystic fibrosis**, and emphysema. It can also be used prior to bronchial studies, such as bronchoscopy, to help clear the airway and is also used as routine tracheostomy care. To manage respiratory symptoms, the medication is inhaled. Acetylcysteine is also administered orally or intravenously as the antidote for acetaminophen toxicity.

Side effects include tachycardia, nausea, and vomiting. Acetylcysteine is contraindicated in clients with hypersensitivity to it or those with peptic ulcer disease.

Dornase Alfa

Dornase alfa is another mucolytic used most often to lower the number of lung infections and help lung function in cystic fibrosis. Dornase alfa acts like an enzyme naturally found in the lungs to help thin out thick, sticky mucus. Removing mucus in these clients helps to reduce the number of infections that they may have by reducing the potential breeding ground for bacteria.

Dornase alfa can cause voice changes, hoarseness, and sore throat. It is contraindicated in those with hypersensitivity to the drug or to Chinese hamster ovary cell products used in the pharmaceutical industry.

Table 24.14 lists common mucolytics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Acetylcysteine (Mucomyst)	*For removal of secretions in clients with cystic fibrosis, bronchitis, and other respiratory disorders:* 1–2 mL of 10%–20% solution inhalant instilled into trachea as often as every hour. *Prior to diagnostic studies:* 2–3 administrations of 1–2 mL of 20% solution inhalant or 2–4 mL of 10% solution inhalant prior to procedure. *For routine tracheostomy care:* 1–2 mL of 10%–20% solution inhalant by direct instillation into tracheostomy every 1–4 hours.
Dornase alfa (Pulmozyme)	2.5 mg of inhalant in nebulizer once daily.

TABLE 24.14 Drug Emphasis Table: Mucolytics (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Mucolytics can cause tachycardia, nausea, and vomiting. Some clients may experience voice changes, hoarseness, and sore throat. Clients with hypersensitivity to mucolytics and those with peptic ulcer disease should avoid these drugs.

Table 24.15 is a drug prototype table for mucolytics featuring acetylcysteine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Mucolytic **Mechanism of Action** Reduces viscosity of pulmonary secretions	**Drug Dosage** *For removal of secretions in clients with cystic fibrosis, bronchitis, and other respiratory disorders:* 1–2 mL of 10%–20% solution inhalant instilled into trachea as often as every hour. *Prior to diagnostic studies:* 2–3 administrations of 1–2 mL of 20% solution inhalant or 2–4 mL of 10% solution inhalant prior to procedure. *Routine tracheostomy care:* 1–2 mL of 10%–20% solution inhalant by direct instillation into tracheostomy every 1–4 hours.
Indications Adjunctive therapy for pneumonia, bronchitis, and cystic fibrosis **Therapeutic Effects** Thins pulmonary secretions and allows for easier clearance	**Drug Interactions** Activated charcoal **Food Interactions** No significant interactions
Adverse Effects Fever Tachycardia Nausea Vomiting Pharyngitis Bronchospasm Dyspnea	**Contraindications** Hypersensitivity Peptic ulcer disease Caution: Older adults with debilitation or severe respiratory insufficiency Asthma (IV form)

TABLE 24.15 **Drug Prototype Table: Acetylcysteine** (source: https://dailymed.nlm.nih.gov/dailymed/)

LINK TO LEARNING

Respiratory Therapy Zone

Access multimedia content (https://openstax.org/books/pharmacology/pages/24-3-expectorants-and-mucolytics)

This video from Respiratory Therapy Zone discusses the mucolytic agent acetylcysteine.

SAFETY ALERT

Mucolytics

Because acetylcysteine commonly causes vomiting, it should be strictly avoided in clients with peptic ulcer disease, esophageal varices, and **Mallory-Weis tears**.

Nursing Implications

The nurse should do the following for clients who are taking expectorants and mucolytics:

- Prior to administering, assess the client's medical history, current drug list, and allergies for potential interactions and contraindications.
- Assess the client's respiratory status for signs of respiratory distress that indicate the need for additional evaluation and treatment. Also, identify the underlying reason for the cough to ensure the client is receiving the appropriate treatment.
- Assess the client's cough including the frequency and amount and type of sputum.
- Educate the client on adverse effects of expectorants including headache, dizziness, nausea, and vomiting.
- Educate the client on adverse effects of mucolytics including fever, tachycardia, and pharyngitis.

- Monitor vital signs for tachycardia or fever for clients taking mucolytics.
- Clients receiving acetylcysteine should be monitored closely for bronchospasm, especially if they have asthma, because they are at higher risk for bronchospasm.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an expectorant or mucolytic should:

- Take the drugs as prescribed and only for the time indicated.
- Be sure to drink fluids to help loosen secretions.
- Increase deep breathing exercises to assist with secretion movement.
- Report any adverse effects.
- Notify the health care provider if symptoms last longer than one week, become worse, or are accompanied by other symptoms.

Chapter Summary

This chapter discussed various upper respiratory medications including antihistamines, decongestants, antitussives, expectorants, and mucolytics. Many of these medications are available over the counter and are widely used by clients. It is important to understand the appropriate use for each of these drugs and how they assist clients with respiratory disorders. Providing appropriate client education for these medications is crucial to ensure safe use and avoidance of adverse effects, especially because many of these medications come in combination products. The nurse should remind clients to check the labels of medications that they are taking to avoid ingesting too much of a particular medication.

Key Terms

antihistamines drugs used to treat symptoms of allergies
antitussives drugs used to relieve nonproductive coughs
cystic fibrosis a genetic condition that causes mucus to be sticky and thick, leading to blockages, damage, and infections
decongestants drugs used to relieve nasal congestion caused by respiratory disorders
expectorants drugs that help to clear mucus from the airway
histamines chemicals in body cells that are responsible for many of the symptoms of allergies
Mallory-Weis tears lacerations in the esophagus or stomach that occur from prolonged vomiting or coughing; often seen in clients with alcohol misuse
methamphetamine a potent central nervous system stimulant mainly used as a recreational drug
monoamine oxidase inhibitors (MAOIs) a class of drugs often used to treat depression and panic disorder
mucolytics drugs that help to clear mucus from the upper and lower airways of the respiratory system
muscarinic a type of receptor in the body that mediates parasympathetic effects such as slow heart rate and increased activity of smooth muscle tissue
rebound congestion constant nasal congestion resulting from overuse of nasal decongestants
urticaria raised itchy rash that appears on the skin

Review Questions

1. A client is asking what medication would be best for relief of their allergies. Upon further assessment, the nurse learns that the client is a construction worker. What should the nurse recommend?
   a. Diphenhydramine
   b. Cetirizine
   c. Brompheniramine
   d. Acetylcysteine

2. A client taking guaifenesin informs the nurse that the medication is not helping with their cough. What further information should the nurse obtain from the client?
   a. “Is your cough productive or nonproductive?”
   b. “What time of day do you take the drug?”
   c. “Have you increased the dose?”
   d. “Why don’t you take another drug?”

3. Acetylcysteine is a mucolytic used to help clear respiratory secretions from the airways. For what other purpose can it be used?
   a. Allergic reactions
   b. Pain management
   c. Acetaminophen toxicity
   d. Opioid overdose

4. What statement by the client indicates an understanding of the education provided for oxymetazoline?
   a. “I should use the spray every day even if my nose is not congested.”
   b. “The drug may take weeks to take full effect.”
   c. “I should not use the drug for more than 3 days.”

d. "The drug may produce many systemic side effects."

5. Clients taking opioid antitussives should be monitored closely for what adverse effect?
   a. Increased heart rate
   b. Insomnia
   c. Diarrhea
   d. Respiratory depression

6. The nurse should educate clients taking dextromethorphan to avoid what?
   a. Grapefruit juice
   b. Orange juice
   c. Tomatoes
   d. Caffeine

7. Which statement best describes the action of nasal decongestants?
   a. Nasal decongestants promote mucus production, leading to easier clearance of nasal passages.
   b. Nasal decongestants inhibit histamine release, reducing nasal congestion and inflammation.
   c. Nasal decongestants exert their effect by constricting blood vessels in the nasal mucosa, relieving congestion.
   d. Nasal decongestants decrease the production of prostaglandins, which results in decreased nasal discharge.

8. Which of the following statements correctly describes the mechanism of action of loratadine?
   a. Loratadine dilates blood vessels in the nasal passages.
   b. Loratadine is a mucolytic.
   c. Loratadine is an H1 receptor antagonist.
   d. Loratadine is a xanthine.

9. The health care provider orders diphenhydramine 50 mg intramuscularly (IM) for a client with an allergic reaction. The vial contains 25 mg/mL. How many milliliters (mL) should the nurse administer?
   a. 0.5 mL
   b. 1.5 mL
   c. 2 mL
   d. 2.5 mL

10. A client is prescribed loratadine 10 mg orally once daily for seasonal allergies. The available tablets are 5 mg each. How many tablets should the client take per dose?
   a. 1 tablet
   b. 2 tablets
   c. 3 tablets
   d. 4 tablets

CHAPTER 25
Lower Respiratory Disorder Drugs

FIGURE 25.1 The lungs are the core of the respiratory system that moves oxygen into the body and waste gases out. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The lower respiratory system (shown in Figure 25.2) plays a crucial role in respiration, allowing the exchange of oxygen and carbon dioxide between the body and the external environment. The lower respiratory system includes the trachea, the lungs, and within the lungs, the bronchi, bronchioles, and alveoli. See Introduction to the Respiratory System for more information on the lower and upper respiratory systems. Various respiratory diseases and disorders can significantly affect the functioning of the lower respiratory system, leading to respiratory distress, impaired lung function, and reduced quality of life. Lower respiratory drugs are a class of medications designed to alleviate symptoms, manage chronic conditions, and improve overall respiratory function.

Respiratory diseases affecting the lower respiratory system can be broadly classified into two categories: obstructive and restrictive lung diseases. Obstructive lung diseases, such as **asthma** and **Chronic obstructive pulmonary disease (COPD)**, are characterized by airflow limitation due to inflammation, bronchoconstriction, and increased mucus production. Asthma affects the lungs, causing repeated episodes of wheezing, breathlessness, and coughing. COPD is a group of diseases including emphysema and chronic bronchitis. Emphysema damages the airways and causes chronic inflammation in the lungs. This makes it very difficult for the person to breathe. Chronic bronchitis is a productive cough of more than 3 months, specifically within a span of 2 years (Widysanto & Mathew, 2022).

Restrictive lung diseases, such as **pulmonary fibrosis**, involve a reduced lung capacity due to impaired lung tissue expansion or chest wall abnormalities (Martinez-Pitre et al., 2023).

Lower respiratory drugs encompass a wide range of pharmacological agents, each targeting specific mechanisms

involved in respiratory diseases. These drugs can be administered via various routes, including inhalation, oral ingestion, and intravenous infusion, depending on the medication's characteristics and the severity of the respiratory condition.

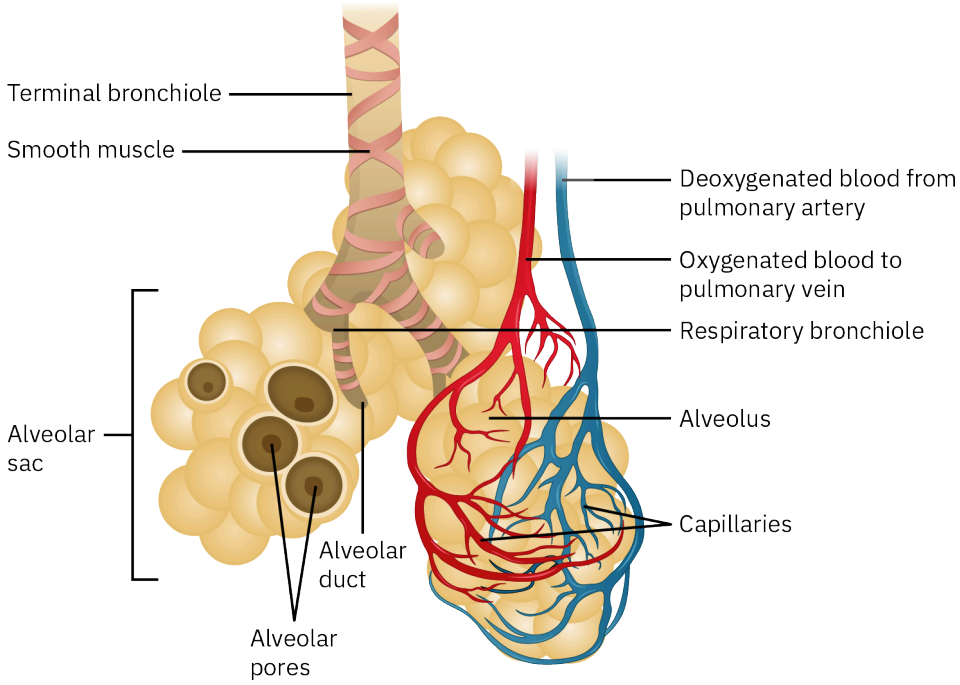


FIGURE 25.2 Bronchioles and alveoli are part of the lower respiratory system. They play a vital role in the exchange of oxygen and carbon dioxide between the body and the external environment. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

25.1 Adrenergics and Anticholinergics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 25.1.1 Discuss the use of adrenergic and anticholinergic drugs used to treat lower respiratory disorders.
- 25.1.2 Explain the indications, actions, adverse reactions, and interactions of adrenergic and anticholinergic drugs used to treat lower respiratory disorders.
- 25.1.3 Describe nursing implications of adrenergic and anticholinergic drugs used to treat lower respiratory disorders.
- 25.1.4 Explain the client education related to adrenergic and anticholinergic drugs used to treat lower respiratory disorders.

Adrenergics

Adrenergic drugs, also known as **sympathomimetic** drugs, are a class of medications that that bind to adrenergic receptors throughout the body. These receptors are stimulated by the neurotransmitters **norepinephrine** and **epinephrine**, also known as adrenaline. Adrenergic drugs mimic the effects of these neurotransmitters or enhance their activity, resulting in a wide range of physiological responses. These medications can act on different types of adrenergic receptors, including alpha-adrenergic receptors and beta-adrenergic receptors, producing diverse effects on various organ systems. Adrenergic drugs are used to manage several conditions, such as asthma, and they play a crucial role in bronchodilation (Farzam et al., 2022).

Beta Adrenergics

Beta-adrenergic drugs target beta-adrenergic receptors in the sympathetic nervous system. These receptors are found in various tissues, including the heart, lungs, and smooth muscles, and lead to smooth muscle relaxation.

One type of beta-adrenergic receptor, beta 2, is predominantly found in the smooth muscles of the lungs, bronchioles, and blood vessels. Stimulating these receptors leads to bronchodilation and vasodilation. Medications like albuterol, levalbuterol, and salmeterol are frequently used in the treatment of respiratory conditions, such as

asthma and COPD, that cause bronchoconstriction.

Albuterol is a short-acting beta-2 adrenergic agonist and is primarily used to treat and manage respiratory conditions such as asthma, COPD, and exercise-induced bronchospasm. Albuterol works by engaging or stimulating the beta-2 adrenergic receptors, relaxing the smooth muscles in the airways and leading to bronchodilation and improved airflow. Albuterol is often used as a rescue medication for acute asthma attacks and as maintenance therapy for COPD (Hsu & Bajaj, 2023).

Levalbuterol and salmeterol are also beta-adrenergic agonists and are used to treat asthma and COPD. Levalbuterol is a short-acting beta-2 agonist, and salmeterol is a long-acting beta-2 agonist. Salmeterol is used as a maintenance therapy to prevent asthma and should not be used for immediate relief of an asthma attack, whereas levalbuterol is used similarly to albuterol.

Table 25.1 lists common beta adrenergics used for lower respiratory system disorders and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Albuterol (Accuneb, Proventil, Ventolin)	*In adults for acute episodes of bronchospasm or prevention of asthmatic symptoms:* 2 inhalations (2.5 mg per inhalation) every 4–6 hours. Some clients may only need 1 inhalation every 4 hours. *In adults for exercise-induced bronchospasm prevention:* 2 inhalations (2.5 mg per inhalation) 15 minutes prior to exercise. *In children age 2–12:* 1.25 mg or 0.63 mg 3–4 times daily via nebulization.
Levalbuterol (Xopenex)	*Adults:* 0.63 mg every 6–8 hours by nebulization. *Children 6–11:* 0.31 mg 3 times per day by nebulization, not to exceed 0.63 mg 3 times a day.
Salmeterol (Serevent)	*For bronchodilation and prevention of asthma symptoms:* 1 inhalation (50 mcg) twice daily, 12 hours apart, in combination with inhaled corticosteroids. *For exercise-induced bronchospasm:* 1 inhalation (50 mcg) 30 minutes prior to exercise. *For COPD:* 1 inhalation (50 mcg) twice daily 12 hours apart.

TABLE 25.1 **Drug Emphasis Table: Beta Adrenergics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects include tremors, nervousness, headache, and tachycardia. Cold symptoms, migraine, chest pain, bronchitis, and nausea have also been reported. Clients with severe cardiac disease should use albuterol only at the direction of their health care provider due to systemic effects on heart rate and blood pressure (DailyMed, *Albuterol sulfate*, 2023).

Table 25.2 is a drug prototype table for beta adrenergics featuring albuterol. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Beta adrenergic **Mechanism of Action** Relaxes bronchial, uterine, and vascular smooth muscle by stimulating beta-2 receptors	**Drug Dosage** *In adults for acute episodes of bronchospasm or prevention of asthmatic symptoms:* 2 inhalations (2.5 mg per inhalation) every 4–6 hours. Some clients may only need 1 inhalation every 4 hours. *In adults for exercise-induced bronchospasm prevention:* 2 inhalations (2.5 mg per inhalation) 15 minutes prior to exercise. *In children ages 2–12:* 1.25 mg or 0.63 mg 3–4 times daily via nebulization.
Indications Prevention and relief of bronchospasm Prevention of exercise-induced bronchospasm **Therapeutic Effects** Bronchodilation Relief of bronchospasm	**Drug Interactions** Antiarrhythmics Beta blockers CNS stimulants **Food Interactions** No significant interactions
Adverse Effects Tremor Nervousness Tachycardia Headache	**Contraindications** Hypersensitivity Caution: Cardiac disorder Hyperthyroidism Diabetes Severe cardiac disease

TABLE 25.2 **Drug Prototype Table: Albuterol** (source: https://dailymed.nlm.nih.gov/dailymed/)

Alpha- and Beta-Adrenergic Agonists

Alpha- and beta-adrenergic agonists stimulate both alpha- and beta-adrenergic receptors. Alpha-adrenergic receptors are found primarily in smooth muscles, regulating vasoconstriction and blood pressure. Beta-adrenergic receptors are present in the heart, lungs, and other tissues and control heart rate, bronchodilation, and metabolic processes.

Ephedrine, a sympathomimetic drug, acts as a nonselective alpha- and beta-adrenergic agonist, meaning it stimulates both types of receptors. The ability of ephedrine to activate both receptor types makes it a widely used drug for conditions such as asthma and nasal congestion as well as low blood pressure. However, its usage requires caution due to potential side effects and interactions with other medications (Drugbank Online, 2023).

Epinephrine is used often as an emergency treatment for allergic reactions and respiratory distress including anaphylaxis. It works by relaxing and opening air passages to allow for easier breathing. It can be given as an oral inhalation, intravenously, subcutaneously, and as an intramuscular injection (Dalal & Grujic, 2023). Epinephrine can cause anxiety, tremors, palpitations, nausea, and headache.

Table 25.3 lists common alpha and beta adrenergics used for lower respiratory system disorders and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Ephedrine (Emerphed, Corphedra)	1–2 tablets (12.5 mg each) every 4 hours as needed. Maximum dose: 12 tablets in 24 hours.
Epinephrine (Adrenalin, Auvi-Q, Epipen, Primatene Mist)	*Inhalation:* 1 inhalation as needed. Wait 1 minute, then take second inhalation. Wait at least 4 hours between doses. Maximum dose: 8 inhalations in 24 hours. *Intramuscular or subcutaneous:* 0.3–0.5 mg (0.3–0.5 mL) of undiluted epinephrine administered in the anterolateral aspect of the thigh, repeated every 5–10 minutes as necessary. Maximum dose: 0.5 mg (0.5 mL) per injection. Intended for severe exacerbation and/or when inhalation is not available.

TABLE 25.3 **Drug Emphasis Table: Alpha and Beta Adrenergics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Ephedrine can cause an increase in heart rate and blood pressure, insomnia, and tremors. Clients who have hypersensitivity or who have been taking a monoamine oxidase inhibitor (MAOI) should not use ephedrine (DailyMed, *Ephedrine hydrochloride*, 2022).

Epinephrine can cause anxiety, restlessness, and headache. Clients may also report chest pain, high blood pressure, dizziness, and difficulty sleeping.

Table 25.4 is a drug prototype table for alpha and beta adrenergics featuring ephedrine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Adrenergic **Mechanism of Action** Relaxes bronchial smooth muscle by stimulating beta-2 receptors Stimulates alpha- and beta-adrenergic receptors in the sympathetic nervous system	**Drug Dosage** 1–2 tablets (12.5 mg per tablet) every 4 hours as needed. Maximum dose: 12 tablets in 24 hours.
Indications Mild/intermittent asthma **Therapeutic Effects** Bronchodilation Relief of bronchospasm	**Drug Interactions** Alpha blockers Beta blockers Cardiac glycosides MAOIs **Food Interactions** No significant interactions
Adverse Effects Nervousness Palpitations Tachycardia Headache	**Contraindications** Angle-closure glaucoma Heart failure Intermittent asthma Cardiovascular disease Hypertension Stroke Caution: Bronchial asthma or emphysema with degenerative heart disease

TABLE 25.4 **Drug Prototype Table: Ephedrine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Anticholinergics

Anticholinergic drugs block the action of **acetylcholine** at muscarinic receptors, which are found in numerous organs and tissues throughout the body. They produce a range of effects such as relaxation of smooth muscles, reduction in secretions, and inhibition of parasympathetic responses. These medications are useful in the treatment of various conditions, including respiratory disorders, overactive bladder, gastrointestinal disorders, and certain neurological conditions.

SAFETY ALERT

Side Effects of Anticholinergics

Anticholinergics should be used with caution due to potential side effects, especially in older adults, who may be more susceptible to adverse reactions like cognitive impairment and increased risk of falls.

Two commonly used respiratory anticholinergics are ipratropium bromide and tiotropium. Ipratropium bromide, often administered via inhalation, acts as a bronchodilator by blocking the action of acetylcholine at the muscarinic receptors in the airways. This helps to relax the smooth muscles and widen the air passages, providing relief from symptoms such as wheezing and shortness of breath in conditions like asthma and COPD.

Tiotropium, also an inhalation medication, is a long-acting anticholinergic that provides sustained bronchodilation by binding specifically to the muscarinic receptors in the airways. It is primarily used for the long-term maintenance treatment of COPD to reduce symptoms and improve lung function.

Table 25.5 lists common anticholinergics used for lower respiratory system disorders and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Ipratropium bromide (Atrovent)	*Metered-dose inhaler (17 mcg):* 4–8 inhalations with spacer every 20 minutes for 3 doses, then hourly as needed for up to 3 hours. *Nebulization (500 mcg)*: 3–4 times daily, with doses 6–8 hours apart.
Tiotropium (Spiriva)	*Hand inhaler:* 2 inhalations of the powder contents of 1 Spiriva capsule, once daily. *Spiriva Respimat inhaler:* For COPD: 2 inhalations (2.5 mcg each) per device actuation once daily. *For asthma:* 2 inhalations (1.25 mcg each) once daily.

TABLE 25.5 **Drug Emphasis Table: Anticholinergics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Side effects of both drugs can include dry mouth, headache, nervousness or dizziness, blurred vision, constipation, and cough. Clients with hypersensitivity, narrow-angle glaucoma, and urinary retention should avoid these drugs; they can cause urinary retention and exacerbate symptoms.

Table 25.6 is a drug prototype table for anticholinergics featuring ipratropium bromide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anticholinergic **Mechanism of Action** Inhibits vagally mediated reflexes by antagonizing acetylcholine at muscarinic receptors on bronchial smooth muscle	**Drug Dosage** *Metered-dose inhaler (17 mcg):* 4–8 inhalations with spacer every 20 minutes for 3 doses, then hourly as needed for up to 3 hours. *Nebulization (500 mcg)*: 3–4 times daily, with doses 6–8 hours apart.
Indications Bronchospasm Relief of acute asthmatic symptoms (when combined with albuterol) **Therapeutic Effects** Bronchodilation Relief of bronchospasm	**Drug Interactions** Other anticholinergics **Food Interactions** No significant interactions
Adverse Effects Dizziness Urinary retention Palpitations Tachycardia Blurred vision Constipation Dry mouth	**Contraindications** Hypersensitivity Caution: Angle-closure glaucoma Bladder neck obstruction Prostatic hyperplasia

TABLE 25.6 **Drug Prototype Table: Ipratropium Bromide** (source: https://dailymed.nlm.nih.gov/dailymed/)

LINK TO LEARNING

Adrenergics

Access multimedia content (https://openstax.org/books/pharmacology/pages/25-1-adrenergics-and-anticholinergics)

In this link to learning, Alila Medical Media presents information on the pharmacology and action of adrenergics. This educational video with animation discusses the different types of adrenergic receptors and the different types of drugs that act on them.

Nursing Implications

The nurse should do the following for clients who are taking adrenergic or anticholinergic drugs:

- Prior to administering, assess the client's medical history, current drug list, and allergies.
- Assess the client's baseline respiratory function.
- Ensure the drug is prepared appropriately using aseptic technique, and verify dosage prior to administration.
- Monitor the client's response to the drug, including any changes in breathing effort, rate, and oxygen saturation.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an adrenergic or anticholinergic drug should:

- Take the drug as prescribed without skipping doses or stopping therapy.
- Prime the inhaler prior to use by shaking it and spraying into the air for a total of 4 sprays. Clean it after use by rinsing it with water and allowing it to dry.

- Wait at least 15 seconds between inhalations if more than one is required.
- Inform the health care provider of worsening symptoms including shortness of breath, cough, chest tightness, and wheezing.
- Create an asthma action plan. The Asthma and Allergy Foundation of America provides an example (https://openstax.org/r/aafa).

The client taking an adrenergic or anticholinergic drug *should not:*

- Use more medication than was prescribed by the health care provider.
- Wash or place a powder inhaler in water.

UNFOLDING CASE STUDY

Part A

Read the following clinical scenario to answer the questions that follow. This case study will evolve throughout the chapter.

Harold Watson is a 65-year-old client who presents to his primary care physician with complaints of worsening shortness of breath, chronic cough, and increased sputum production over the past few months. He reports that these symptoms have significantly impacted his daily activities, and he has also noticed a decrease in his ability to perform simple tasks around the house. Harold reports that he quit smoking 10 years ago but was a heavy smoker for 30 years. He reports smoking roughly one pack of cigarettes per day when he was smoking.

History
Hypertension

Current Medications
Metoprolol 100 mg daily

Vital Signs		Physical Examination
Temperature:	98.7°F	• *Head, eyes, ears, nose, throat (HEENT):* Denies any changes in vision. No difficulty hearing. • *Cardiovascular:* S1, S2 noted. Denies chest pain. Capillary refill less than 3 seconds. • *Respiratory:* Decreased breath sounds in the lower lung fields, prolonged expiration and mild wheezing. • *GI:* Abdomen soft, nontender, nondistended; bowel sounds present in all four quadrants. • *GU:* Denies difficulty with urination. • *Neurological:* Alert and oriented ×4. Denies any dizziness, numbness, or tingling in extremities. • *Integumentary:* No wounds noted.
Blood pressure:	145/90 mm Hg	
Heart rate:	92 beats/min	
Respiratory rate:	20 breaths/min	
Oxygen saturation:	91% on room air	
Height:	5'6"	
Weight:	175 lb	

TABLE 25.7

1. Based on the assessment of Harold, what diagnosis should the nurse anticipate from the health care provider?
   a. Elevated blood pressure
   b. COPD
   c. Allergic reaction
   d. Bronchospasm

2. Based on Harold's past medical history of chronic obstructive pulmonary disease (COPD) and the physical

examination, which of the following medications would be the highest priority to administer to him?

a. Salmeterol
b. Ipratropium bromide
c. Tiotropium
d. Ephedrine

25.2 Corticosteroids

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 25.2.1 Identify the characteristics of corticosteroid drugs used to treat respiratory disorders.
- 25.2.2 Explain the indications, actions, adverse reactions, and interactions of corticosteroid drugs used to treat respiratory disorders.
- 25.2.3 Describe nursing implications of corticosteroid drugs used to treat respiratory disorders.
- 25.2.4 Explain the client education related to corticosteroid drugs used to treat respiratory disorders.

Corticosteroids, specifically inhaled corticosteroids (ICs), play a vital role in the management of respiratory conditions such as asthma and COPD. These medications are designed to reduce inflammation and suppress the immune response in the airways (see Figure 25.3) (Cleveland Clinic, 2023a). By targeting the underlying inflammation, corticosteroids help to control symptoms, prevent exacerbations, and improve lung function. Inhaled corticosteroids are typically administered through inhalation devices directly into the lungs, allowing for targeted delivery to the respiratory system while minimizing systemic side effects. They are considered a cornerstone of long-term respiratory treatment, often used in combination with other bronchodilators for optimal control (Williams, 2018).

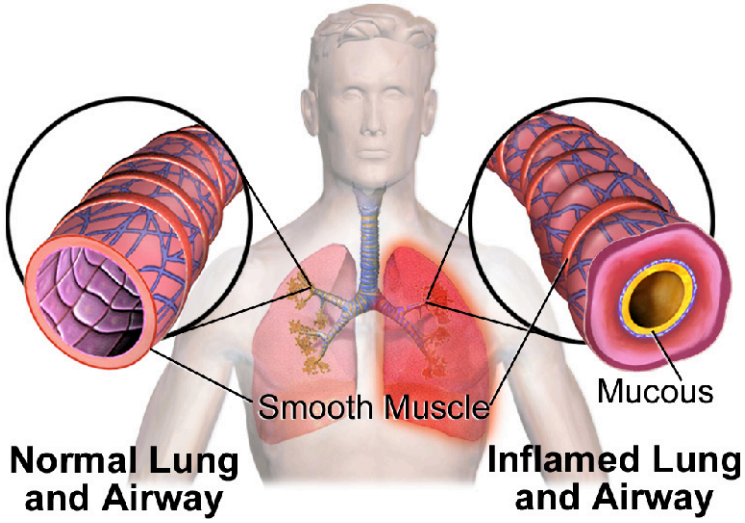


FIGURE 25.3 Corticosteroids work to reduce inflammation in the lungs and airway. (credit: "Medical gallery of Blausen Medical 2014" by Blausen.com staff (2014), *WikiJournal of Medicine 1*(2), DOI:10.15347/wjm/2014.010. ISSN 2002-4436/Wikimedia Commons, CC BY 3.0)

Table 25.8 lists common corticosteroids used for lower respiratory system disorders and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Beclomethasone (Beclovent, Qvar)	40–80 mcg twice daily by oral inhalation, approximately 12 hours apart.
Prednisone (Deltasone, Prednicot, Sterapred)	Initial dose: 5–60 mg orally daily in single dose or as 2–4 divided doses. Maintenance dosage is given daily or every other day (immediate release only). Use lowest dose that will maintain adequate clinical response. Dosage must be individualized, and constant monitoring is needed.

TABLE 25.8 **Drug Emphasis Table: Corticosteroids** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Methylprednisolone (Medrol, Solumedrol)	*Oral:* 4–48 mg daily depending on the disease treated. After favorable response is noted, determine maintenance dosage by decreasing until lowest dosage that will maintain adequate clinical response is achieved. *Intramuscular:* 4–120 mg acetate daily. *Intramuscular or intravenous (IV):* 10–40 mg succinate, with subsequent doses dictated by client's clinical response and condition. This medication should be used for more acute situations, like exacerbations.
Fluticasone (Flovent HFA)	88 mcg (2 inhalations of 44 mcg fluticasone propionate) twice daily by oral inhalation, approximately 12 hours apart.
Budesonide (Pulmicort)	Recommended initial dose: 360 mcg twice daily by oral inhalation. In some adult clients, an initial dose of 180 mcg twice daily may be adequate. Maximum dose: 720 mcg twice daily.

TABLE 25.8 Drug Emphasis Table: Corticosteroids (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Side effects of corticosteroid drugs include **candidiasis** (an oral fungal infection), hoarseness, cough, and increased susceptibility to infection. Clients should not stop corticosteroids abruptly because **adrenal insufficiency** may occur. Those with hypersensitivity to the drug, systemic fungal infections, and recent live vaccines should not use corticosteroids. Corticosteroids can affect potassium levels and sleep patterns, so both should be monitored during treatment. Corticosteroids can also cause weight gain, so weight should be monitored. Corticosteroids can modulate the immune system, so clients should be educated on signs and symptoms of infection to report (Cleveland Clinic, 2023a).

Table 25.9 is a drug prototype table for corticosteroids featuring prednisone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Corticosteroid **Mechanism of Action** Anti-inflammatory effects primarily by stabilizing the membranes of leukocyte lysosomes, reducing inflammation Suppresses the immune response Stimulates bone marrow activity Has an impact on protein, fat, and carbohydrate metabolism	**Drug Dosage** Initial dose: 5–60 mg orally daily in single dose or as 2–4 divided doses. Maintenance dosage is given daily or every other day (immediate release only). Use lowest dose that will maintain adequate clinical response. Dosage must be individualized, and constant monitoring is needed.
Indications Asthmatic conditions COPD **Therapeutic Effects** Decrease in inflammation leading to fewer bronchospasm symptoms	**Drug Interactions** Antidiabetic drugs Nonsteroidal anti-inflammatory drugs (NSAIDs) Cyclosporine **Food Interactions** No significant interactions
Adverse Effects Headache Oral candidiasis Weight gain Hypokalemia GI upset/ulcer risk Hyperglycemia Insomnia Mood disturbances	**Contraindications** Hypersensitivity Caution: Recent myocardial infarction Gastrointestinal ulcer Hypertension Osteoporosis Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

TABLE 25.9 **Drug Prototype Table: Prednisone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking corticosteroid drugs:

- Assess for hypersensitivity.
- Monitor blood pressure, sleep patterns, and potassium levels.
- Weigh client regularly and report weight gain.
- Monitor glucose levels in clients with diabetes.
- Monitor for signs and symptoms of infection.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a corticosteroid should:

- Take the drug as prescribed without skipping doses or stopping therapy.
- Take oral corticosteroids with food to avoid gastrointestinal (GI) upset.
- Rinse mouth out after inhalation corticosteroids to reduce risk of candidiasis (thrush).
- Report all adverse reactions including weight gain, GI upset, sleep disturbances, and mood disturbances.
- Report any signs of infection such as fever or sore throat.
- Weigh themselves daily. Report a weight gain of more than 2–3 pounds over 24 hours or 5 pounds in a week.

- Monitor glucose carefully (if they have diabetes).
- Wear a medical ID bracelet indicating use of corticosteroids.

The client taking a corticosteroid *should not:*

- Stop taking the drug abruptly because this can lead to adrenal insufficiency. Drug will need to be reduced gradually, especially after long-term therapy.

UNFOLDING CASE STUDY

Part B

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up to Case Study Part A.

Harold Watson's health care provider calls him at home to discuss the results of his x-ray. The provider confirms the diagnosis of COPD and discusses a treatment plan with Harold. Part of the plan is a prescription for a beclomethasone inhaler.

3. Harold asks the provider how beclomethasone will help his COPD. Which response by the provider is accurate?
   a. "It will reduce the inflammation in your airways."
   b. "This medication should be used only when you have trouble breathing."
   c. "You can stop using this medication when you feel better."
   d. "This medication will reverse the damage to your lungs."

4. The provider educates Harold to rinse his mouth after using the inhaler. Why does he need to rinse his mouth?
   a. To help avoid allergic reaction
   b. To get rid of the taste
   c. To help the medication absorb
   d. To help prevent candidiasis

25.3 Xanthines, Leukotriene Modifiers, and Mast Cell Stabilizers

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 25.3.1 Identify the characteristics of xanthines, leukotriene modifiers, and mast cell stabilizers used to treat respiratory disorders.
- 25.3.2 Explain the indications, actions, adverse reactions, and interactions of xanthines, leukotriene modifiers, and mast cell stabilizers used to treat respiratory disorders.
- 25.3.3 Describe nursing implications of xanthines, leukotriene modifiers, and mast cell stabilizers used to treat respiratory disorders.
- 25.3.4 Explain the client education related to xanthines, leukotriene modifiers, and mast cell stabilizers used to treat respiratory disorders.

Xanthines

Xanthines are a class of drugs that have been used for many years to manage respiratory conditions, particularly asthma and COPD. Xanthines work by relaxing the smooth muscles in the airways, which helps to open the bronchial passages and improve breathing. They also have some anti-inflammatory effects and can enhance the contractility of the diaphragm.

The primary xanthine medication used in clinical practice is theophylline. Aminophylline is another xanthine that can be used to treat asthma and COPD; however, it has a very narrow therapeutic index and even with regular monitoring can lead to adverse effects.

Theophylline is typically administered orally or intravenously (Khan, 2021). It has a narrow therapeutic window,

requiring careful monitoring of blood levels to ensure efficacy and prevent toxicity. The therapeutic serum levels of theophylline are 10–20 mcg/mL. Doses should be adjusted so that levels are maintained at the lowest level within this range that produces a symptomatic response (DailyMed, *Theophylline*, 2023). Clients with theophylline toxicity may present with abdominal pain, blurred vision, confusion, nausea, and vomiting. Although the use of xanthines has decreased with the advent of newer medications, they still play a role in certain situations and can be a valuable option for clients who do not respond well to other treatments. Clients taking theophylline should avoid other CNS stimulants such as caffeine (Cunha, 2021).

Table 25.10 lists common xanthines used for lower respiratory system disorders and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Theophylline (Theobid, Theo-24)	*Parenteral theophylline (preferred route) for acute bronchospasm in clients not currently receiving theophylline:* Loading dose: 4.6 mg/kg of ideal body weight IV over 30 minutes, then maintenance infusion of 400–1600 mg/day. *Adults over age 60:* 0.3 mg/kg/hour IV, up to a maximum of 17 mg/hour. *Oral theophylline for acute bronchospasm in clients not currently receiving theophylline:* *Adults age 60 and younger:* 5 mg/kg orally, then 300 mg (immediate-release solution/elixir) orally daily in divided doses every 6–8 hours for 3 days. If tolerated, increase to 400 mg orally daily in divided doses every 6–8 hours. If necessary, dosage may be increased after 3 days to 600 mg orally daily in divided doses every 6–8 hours.
Aminophylline (Norphyl, Phyllocontin, Quibron-T)	Loading dose: 4.6 mg/kg of ideal body weight IV over 30 minutes, then maintenance infusion of 0.4 mg/kg/hour up to a maximum of 900 mg/day unless higher doses are required to reach a target level of 10 mcg/mL. *Adults over age 60:* 0.3 mg/kg/hour IV, up to a maximum of 400 mg/day unless higher doses required to reach a target level of 10 mcg/mL.

TABLE 25.10 Drug Emphasis Table: Xanthines (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Close monitoring and individualized dosing are essential when utilizing xanthines in respiratory therapy. Xanthines can have a variety of potential adverse effects, including nausea, vomiting, restlessness, nervousness, increased heart rate, and tremors. The number of adverse effects is partly why xanthines are not as widely used as they formerly were. Clients with hypersensitivity, seizure disorder, hyperthyroidism, and severe cardiac arrhythmias should not use xanthines (Khan, 2021).

Table 25.11 is a drug prototype table for xanthines featuring theophylline. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Xanthine **Mechanism of Action** Relaxes the smooth muscles located in the bronchial airways and pulmonary blood vessels	**Drug Dosage** *Parenteral theophylline (preferred route) for acute bronchospasm in clients not currently receiving theophylline:* Loading dose: 4.6 mg/kg of ideal body weight IV over 30 minutes, then maintenance infusion of 400–1600 mg/day. *Adults older than age 60:* 0.3 mg/kg/hour IV, up to a maximum of 17 mg/hour. *Oral theophylline for acute bronchospasm in clients not currently receiving theophylline:* *Adults age 60 and younger:* 5 mg/kg orally, then 300 mg (immediate-release solution/elixir) orally daily in divided doses every 6–8 hours for 3 days. If tolerated, increase to 400 mg orally daily in divided doses every 6–8 hours. If necessary, dosage may be increased after 3 days to 600 mg orally daily in divided doses every 6–8 hours.
Indications Acute and chronic bronchospasm **Therapeutic Effects** Bronchodilation	**Drug Interactions** Allopurinol Calcium channel blockers Macrolides Methotrexate Nicotine St. John's wort Many others (see drug reference for full list) **Food Interactions** Caffeine Alcohol High-carbohydrate, low-protein diet
Adverse Effects Dizziness Restlessness Headache Palpitations Tachycardia Nausea Vomiting Diarrhea	**Contraindications** Hypersensitivity Peptic ulcer Poorly controlled seizure disorder Caution: Older adults COPD Liver disease Diabetes

TABLE 25.11 **Drug Prototype Table: Theophylline** (source: https://dailymed.nlm.nih.gov/dailymed/)

Leukotriene Modifiers

Leukotriene modifiers, also known as leukotriene receptor antagonists or leukotriene inhibitors, are a class of medications used to manage various inflammatory conditions, particularly asthma. These medications target **leukotrienes**, which are inflammatory substances produced in the body in response to certain triggers. By blocking the effects of leukotrienes, leukotriene modifiers help to reduce inflammation, bronchoconstriction, and mucus production in the airways. This can lead to improved asthma control, decreased frequency of asthma symptoms, and reduced need for rescue medications.

Leukotriene modifiers, such as montelukast, zafirlukast, and zileuton, are typically administered orally and are often

used as adjunctive therapy in combination with other asthma medications. Montelukast is taken at night due to its short half-life and to ensure peak drug levels with symptom onset (Cleveland Clinic, 2023b).

Table 25.12 lists common leukotriene modifiers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Montelukast (Singulair)	One 10 mg tablet orally daily, in the evening.
Zafirlukast (Accolate)	One 20 mg tablet orally twice daily.
Zileuton (Zyflo, Zyflo CR)	Two 600 mg tablets orally twice daily within 1 hour after morning and evening meals; total dose: 2400 mg.

TABLE 25.12 **Drug Emphasis Table: Leukotriene Modifiers** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Montelukast is typically well tolerated; side effects include fever, headache, cough, abdominal pain, and diarrhea. Clients with hypersensitivity should not take this drug. Zafirlukast can cause headache, nausea, diarrhea, dizziness, and vomiting. Zileuton's most common adverse effects are sinusitis and nausea. Both zafirlukast and zileuton should be avoided in clients who are hypersensitive and in clients with hepatic impairment.

Table 25.13 is a drug prototype table for leukotriene modifiers featuring montelukast. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Leukotriene modifier **Mechanism of Action** Decreases action of leukotrienes	**Drug Dosage** One 10 mg tablet orally daily, in the evening.
Indications Asthma Exercise-induced bronchospasm **Therapeutic Effects** Reduced asthmatic symptoms	**Drug Interactions** Gemfibrozil **Food Interactions** No significant interactions
Adverse Effects Headaches Dizziness Epistaxis Urticaria	**Contraindications** Hypersensitivity Caution: Montelukast is linked to psychological reactions such as agitation, aggression, depression, and suicidal thinking. It should be used cautiously in clients with mental health disorders and under supervision of the health care provider.

TABLE 25.13 **Drug Prototype Table: Montelukast** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Montelukast

Serious neuropsychiatric events have been reported in clients taking montelukast. Agitation, hostile and/or aggressive behavior, depression, and suicidality have been seen.

Mast Cell Stabilizers

Mast cell stabilizers are medications used to manage allergic conditions such as asthma and allergic rhinitis. These medications work by preventing the release of inflammatory substances, particularly **histamine**, from **mast cells**. Histamine is a key mediator of allergic reactions and is responsible for the symptoms of itching, sneezing, wheezing, and swelling. By stabilizing mast cells, mast cell stabilizers help to inhibit the release of histamine and other inflammatory mediators, thereby reducing the allergic response.

Cromolyn sodium is one of the commonly used mast cell stabilizers. It is available as an inhaler for asthma and is most effective when used prophylactically, before exposure to triggers, because it does not provide immediate relief of symptoms (Science Direct, 2019).

Adverse Effects and Contraindications

Mast cell stabilizers are generally well tolerated, with minimal systemic absorption and few side effects. Side effects that may occur include coughing, sneezing, nausea, wheezing, and nasal congestion. Clients with a hypersensitivity to the drug should not take cromolyn (DailyMed, *Cromolyn sodium*, 2022).

Table 25.14 is a drug prototype table for mast cell stabilizers featuring cromolyn sodium (Intal). It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Mast cell stabilizer **Mechanism of Action** Inhibits the release of mediators from mast cells Indirectly blocks calcium ions from entering the mast cell, thereby preventing mediator release	**Drug Dosage** 1 ampule (20 mg/2 mL) administered by nebulization 4 times daily at regular intervals.
Indications Asthma symptom prophylaxis **Therapeutic Effects** Reduced incidence of asthmatic symptoms	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Headache Diarrhea Nausea Myalgia Rash Abdominal pain	**Contraindications** Hypersensitivity

TABLE 25.14 **Drug Prototype Table: Cromolyn Sodium** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking xanthines, leukotriene modifiers, and mast cell stabilizers:

- Assess for hypersensitivity.
- Ensure the client's medication list is up to date.
- Monitor for signs and symptoms of toxicity including blurred vision, nausea and vomiting, headache, and confusion.
- For leukotriene modifiers, assess for neuropsychiatric symptoms including depression, hallucinations, suicidal thoughts, and anxiety.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a xanthine, leukotriene modifier, or mast cell stabilizer should:

- Take the drug as prescribed without skipping doses or stopping therapy, even if asymptomatic.
- Report all adverse reactions including headache, diarrhea, nausea, abdominal pain, irritability, and suicidal thoughts.
- Report any worsening symptoms including shortness of breath, wheezing, or increase in allergy symptoms such as runny nose and itchy, watery eyes.
- Take drug with water and/or food to minimize GI distress.
- Keep appointments for lab draws to monitor medication levels.

The client taking a xanthine, leukotriene modifier, or mast cell stabilizer *should not:*

- Stop taking the drug abruptly.
- Use these medications as rescue medications in acute asthma attacks.

Chapter Summary

This chapter provided an overview of various medications commonly used in the management of lower respiratory conditions: adrenergic drugs, anticholinergics, corticosteroids, xanthines, leukotriene modifiers, and mast cell stabilizers.

The chapter provided an understanding of the different classes of respiratory medications and their mechanisms of action. Each medication class has its unique role in managing lower respiratory conditions, and a combination of these medications may be used for optimal control of symptoms, prevention of exacerbations, and improved quality of life for clients with lower respiratory conditions. Health care professionals should carefully consider the client's individual needs, characteristics, and treatment goals when selecting and prescribing these medications.

Key Terms

acetylcholine a neurotransmitter that contracts smooth muscles, dilates blood vessels, increases bodily secretions, and reduces heart rate

adrenal insufficiency caused when the adrenal glands do not manufacture sufficient quantities of cortisol

adrenergic refers to the activation or stimulation of the adrenergic receptors in the sympathetic nervous system

alpha- and beta-adrenergic agonists a class of drugs that stimulate all adrenergic receptors

anticholinergic drugs drugs that inhibit the action of acetylcholine

asthma a respiratory disease that affects the lungs and causes repeated episodes of wheezing, breathlessness, and coughing

beta adrenergic activation or stimulation of beta-adrenergic receptors, which are found in various tissues throughout the body

candidiasis fungal infection caused by a yeast called *Candida*

chronic obstructive pulmonary disease (COPD) group of diseases that cause airflow blockage and breathing problems; includes emphysema and chronic bronchitis

corticosteroids anti-inflammatory medications used for a wide range of conditions

epinephrine a neurotransmitter and hormone, also known as adrenaline; also used as a medication

histamine a chemical in the body that causes many symptoms of allergies such as runny nose or sneezing

leukotriene modifiers medications that inhibit leukotriene-related enzymes and oppose inflammatory mediators

leukotrienes a group of inflammatory mediators that are primarily responsible for bronchoconstriction

mast cell stabilizers prevent mast cell degranulation and mediator release

mast cells cells that play a role in the immune system and help control immune responses; contain chemicals such as histamine

norepinephrine neurotransmitter and hormone as well as a medication that is used to increase and maintain blood pressure

pulmonary fibrosis a lung disease that occurs when lung tissue becomes damaged and scarred, making it difficult for lungs to work properly

sympathomimetic producing physiological effects characteristic of the sympathetic nervous system by promoting the stimulation of sympathetic nerves

xanthines class of compounds derived from purine that have stimulant properties and can relax airway smooth muscle

Review Questions

1. A nurse is caring for a client with acute bronchospasm. The health care provider orders albuterol, a short-acting beta-2 adrenergic agonist. What is the most appropriate rationale for administering albuterol to the client?
   a. To reduce airway inflammation
   b. To stimulate cholinergic receptors
   c. To induce bronchodilation
   d. To suppress the immune response

2. A client is ordered 60 mg of prednisone daily to be taken in three divided doses. How much will the client take for each dose?
   a. 20 mg
   b. 15 mg

c. 30 mg
d. 10 mg

3. A nurse is reviewing the medication regimen of a client with asthma. The client is prescribed theophylline, a xanthine derivative. The nurse understands that theophylline is primarily used for what particular purpose?
a. Acute relief of bronchospasm
b. Prevention of exercise-induced asthma
c. Long-term control of asthma symptoms
d. Reduction of airway inflammation

4. A nurse is caring for a client with COPD who is prescribed ipratropium bromide, a respiratory anticholinergic medication. What is the most appropriate rationale for administering ipratropium bromide to the client?
a. To reduce airway inflammation
b. To stimulate cholinergic receptors
c. To induce bronchodilation
d. To suppress the immune response

5. The loading dose of theophylline is 4.6 mg/kg. The client for whom it is prescribed weighs 121 pounds. How much will the nurse give for the loading dose?
a. 125 mg
b. 155 mg
c. 250 mg
d. 253 mg

6. A nurse is providing education to a client prescribed montelukast, a leukotriene modifier, for the management of asthma. The nurse informs the client about potential side effects of this medication. Which side effect should the nurse include in the client education?
a. Dry mouth and blurred vision
b. Increased heart rate and palpitations
c. Headache and dizziness
d. Excessive drowsiness and sedation

7. A nurse is assessing a client who has been prescribed a respiratory anticholinergic medication. What medical history would be a concern for this nurse when administering the anticholinergic medication?
a. History of hypertension
b. History of osteoarthritis
c. History of migraines
d. History of urinary retention

8. A nurse is educating a client who has been taking methylprednisolone for an extended period. The nurse emphasizes the importance of gradually tapering the medication instead of abruptly stopping it. Which risk is the nurse concerned about?
a. Allergic reactions
b. Gastrointestinal bleeding
c. Adrenal insufficiency
d. Neurological impairment

9. A nurse is providing education to a client who has been prescribed salmeterol, a long-acting beta-2 adrenergic agonist. The nurse instructs the client on the proper use of the medication. Which of the following statements by the client indicates a need for further education?
a. “I should use salmeterol for quick relief during an asthma attack.”
b. “I will rinse my mouth after using the inhaler to prevent throat irritation.”
c. “Salmeterol is a long-acting medication that helps prevent asthma symptoms.”

d. “I should not exceed the prescribed dosage of salmeterol in a 24-hour period.”

10. A nurse is caring for a client who has been prescribed tiotropium, an anticholinergic medication used to manage COPD. The nurse provides education to the client regarding the medication. Which of the following statements made by the client indicates an understanding of tiotropium?

a. “This medication will help reduce airway inflammation.”
b. “I should take this medication during an acute COPD exacerbation.”
c. “Tiotropium works by relaxing the muscles in my airways.”
d. “I can take an extra dose of tiotropium if I experience worsening symptoms.”

CHAPTER 26

Hypothalamus, Pituitary, and Adrenal Disorder Drugs

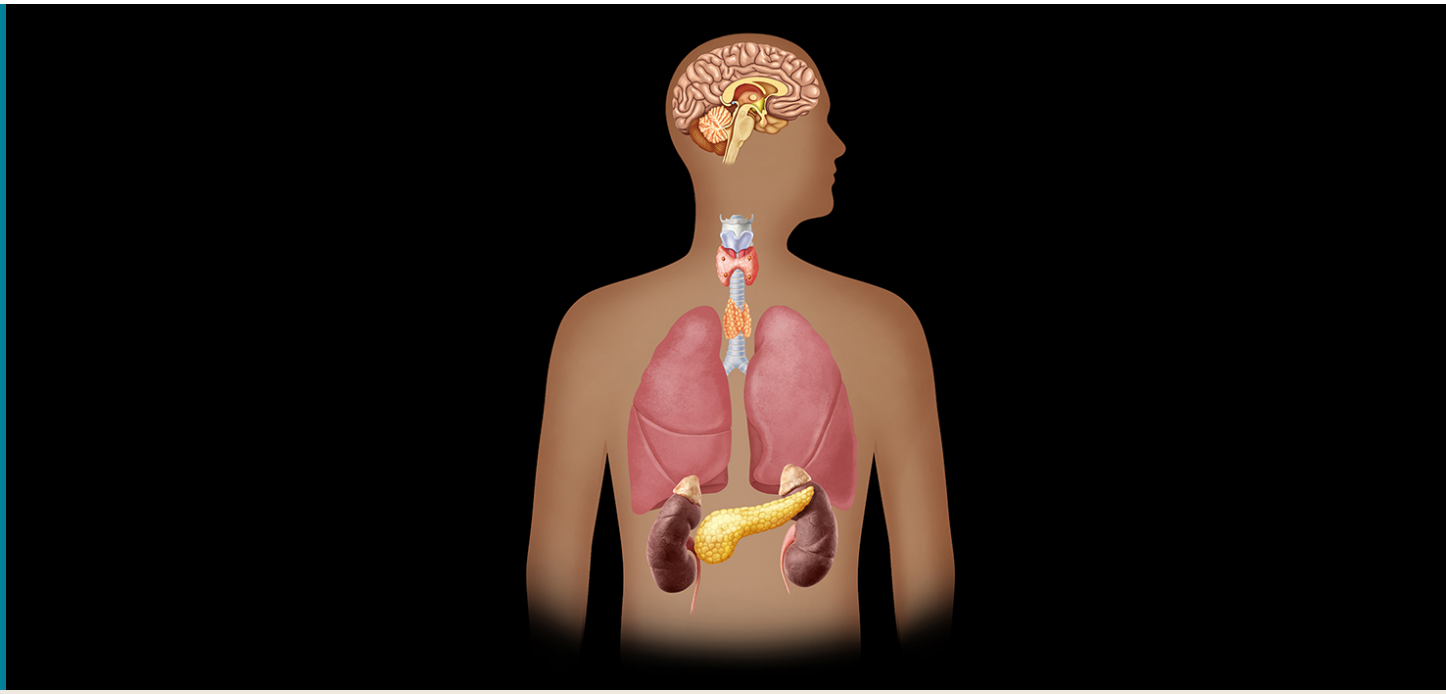


FIGURE 26.1 The endocrine system regulates all biological processes related to development of the brain and nervous system, reproduction, growth, and metabolism. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The **endocrine system** serves as a crucial communication network within the body, regulating important functions such as growth and development, reproduction, energy use, and electrolyte balance. The endocrine system closely interacts with the nervous system to maintain **homeostasis** and ensure adequate responses to various stressors. This chapter will cover the pharmacologic agents utilized for managing endocrine disorders affecting the hypothalamus, pituitary gland, and adrenal cortex.

26.1 Introduction to the Adrenal Cortex, Pituitary, and Hypothalamus

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 26.1.1 Describe the function of the hypothalamus, pituitary gland, and adrenal cortex.
- 26.1.2 Discuss hormones associated with the hypothalamus, pituitary gland, and adrenal cortex.

Introduction to the Hypothalamus

The **hypothalamus** is critical to coordinating both nervous and endocrine responses to internal and external stimuli, making it a crucial component of the **neuroendocrine system**, which is central to regulatory function, as can be seen in Figure 26.2. This section will delve into the intricacies of the hypothalamus by exploring its functions and the

hormones it produces.

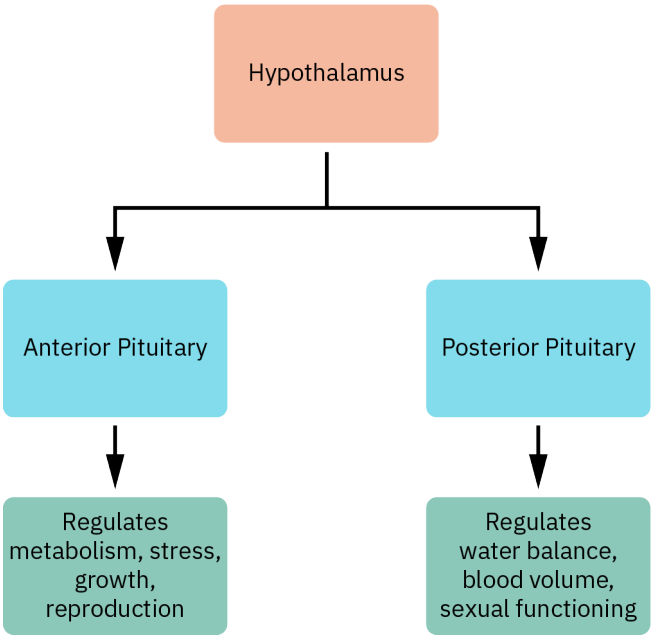


FIGURE 26.2 The hypothalamus coordinates neuroendocrine responses from different functions throughout the body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Hypothalamus Function

The hypothalamus gland is located at the base of the forebrain—above the pituitary gland—and serves as a critical regulatory center in the body, responsible for coordinating both nervous and endocrine functions. The hypothalamus controls a range of essential physiological processes, including body temperature, hunger and thirst, water and electrolyte balance, blood pressure, heart rate, sleep and wake cycles, and reproductive behaviors. Additionally, the hypothalamus plays a crucial role in regulating the release of hormones from the pituitary gland, which controls many endocrine functions throughout the body.

Hypothalamus Hormones

The hypothalamus produces and releases several hormones, which play important roles in regulating various physiological processes in the body (Shahid et al., 2022). Some of the major hypothalamus hormones are included in Table 26.1. These hormones are released into the bloodstream and travel to their target organs or glands, where they stimulate or inhibit the release of other hormones or regulate various physiological processes.

Releasing Hormone	Associated Hormones	Effect
Stimulating Hormones		
Gonadotropin-releasing hormone (GnRH)	Luteinizing hormone (LH) Follicle-stimulating hormone (FSH)	Stimulates gamete production and androgen production, which regulates reproductive functions
Thyrotropin-releasing hormone (TRH)	Thyroid-stimulating hormone (TSH)	Stimulates the thyroid gland to produce hormones and helps to regulate metabolism
Corticotropin-releasing hormone (CRH)	Adrenocorticotropic hormone (ACTH)	Stimulates the adrenal glands to produce cortisol, a stress hormone
Growth hormone–releasing hormone (GHRH)	Growth hormone	Promotes growth and development
Prolactin-releasing hormone (PRH)	Prolactin (PRL)	Promotes lactation from the mammary glands
Inhibitory Hormones		

TABLE 26.1 **Hypothalamus Hormones: Releasing and Associated Hormones with Their Effects**

Releasing Hormone	Associated Hormones	Effect
Prolactin-inhibiting hormone (PIH)	PRL	Inhibits the release of PRL from the pituitary gland
Somatostatin	Growth hormone TSH	Inhibits the release of growth hormone and TSH from the anterior pituitary gland

TABLE 26.1 Hypothalamus Hormones: Releasing and Associated Hormones with Their Effects

Introduction to the Pituitary Gland

The **pituitary gland** (see Figure 26.3), or pituitary, is a small, pea-sized gland that is a vital part of the endocrine system, regulating various physiological functions in the body. The pituitary, also known as the **hypophysis**, is located at the base of the brain and is often referred to as the "master gland" because it controls the secretion of hormones by many other glands. The pituitary is divided into two parts, the anterior pituitary and the posterior pituitary, each with unique functions and hormone secretions (Alatzoglou et al., 2020).

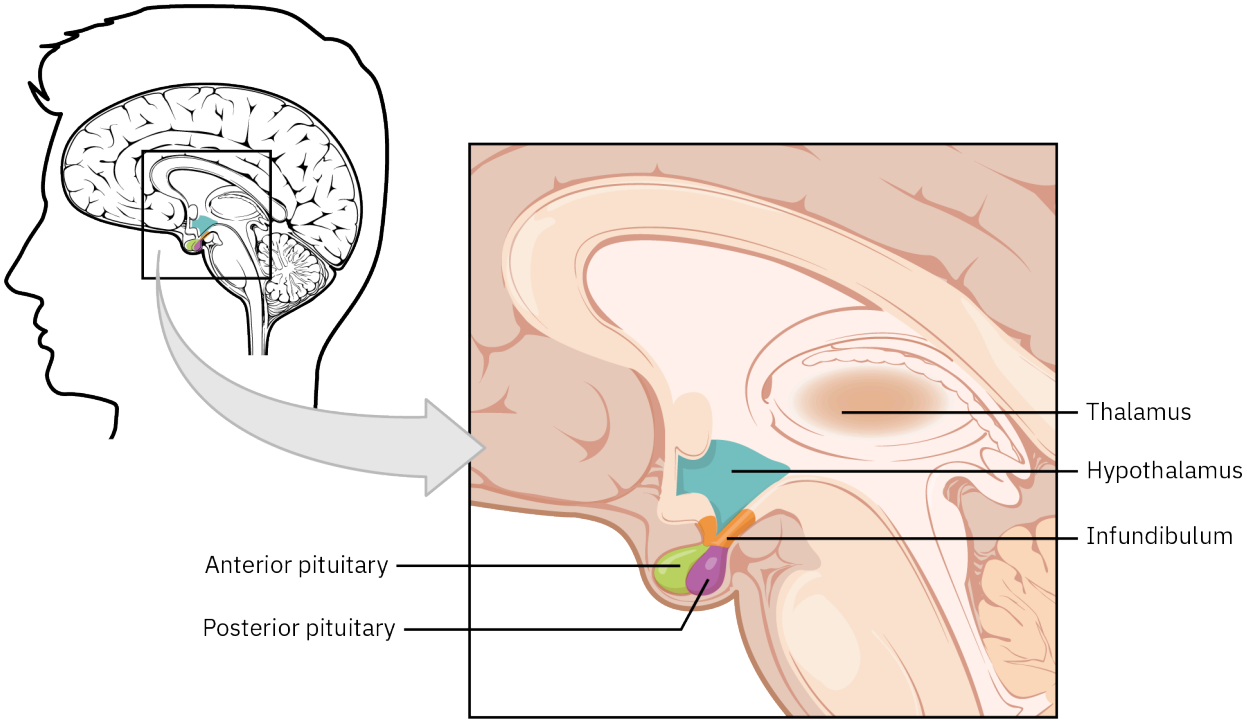


FIGURE 26.3 The pituitary gland sits at the base of the brain and is considered the "master gland" because of its hormone regulatory actions. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The anterior pituitary, also known as the **adenohypophysis**, is the front part of the pituitary. The adenohypophysis is composed of different types of cells that secrete various hormones (see the following section). The anterior pituitary hormones play essential roles in regulating growth and development, metabolism, reproduction, and stress response (Alatzoglou et al., 2020).

The posterior pituitary, also known as the **neurohypophysis**, is the back part of the pituitary. Unlike the anterior pituitary, it does not synthesize its own hormones, but stores and releases two hormones produced by the hypothalamus: oxytocin and **antidiuretic hormone** (ADH), also known as human **vasopressin**. Oxytocin is involved in the contraction of the uterus during childbirth and breast milk ejection during breastfeeding. ADH regulates water balance in the body by controlling the amount of water reabsorbed in the kidneys (Alatzoglou et al., 2020).

Pituitary Function

The pituitary's primary function is to produce and secrete hormones that act on various organs and tissues throughout the body. Overall, the pituitary assists in regulating various bodily processes and maintaining homeostasis in the body.

Pituitary Hormones

Some of the major hormones produced by the pituitary include:

- *Growth hormone (GH):* Promotes the growth and development of bones, muscles, and organs
- *Prolactin (PRL):* Stimulates breast milk production
- *Thyroid-stimulating hormone (TSH):* Regulates the function of the thyroid gland
- *Adrenocorticotropic hormone (ACTH):* Stimulates the adrenal cortex to produce cortisol, which helps the body respond to stress
- *Follicle-stimulating hormone (FSH):* Stimulates the development of eggs in females and sperm in males
- *Luteinizing hormone (LH):* Regulates the production of sex hormones, including estrogen and testosterone

Introduction to the Adrenal Cortex

The **adrenal glands**, which are located on top of each kidney, consist of two layers: the adrenal medulla and the adrenal cortex. The adrenal medulla is the inner layer of the adrenal glands and is important for producing epinephrine and norepinephrine in response to stress. This chapter, however, will focus on the **adrenal cortex** as it relates to endocrine function. The adrenal cortex, as is seen in Figure 26.4, is the outer layer of the adrenal glands. The adrenal cortex produces several important hormones that are essential for proper functioning of the body. Each of the three layers of the adrenal cortex produces a different hormones. The outermost layer is called the **zona glomerulosa**; the middle layer is called the **zona fasciculate**; and the innermost layer is called the **zona reticularis**.

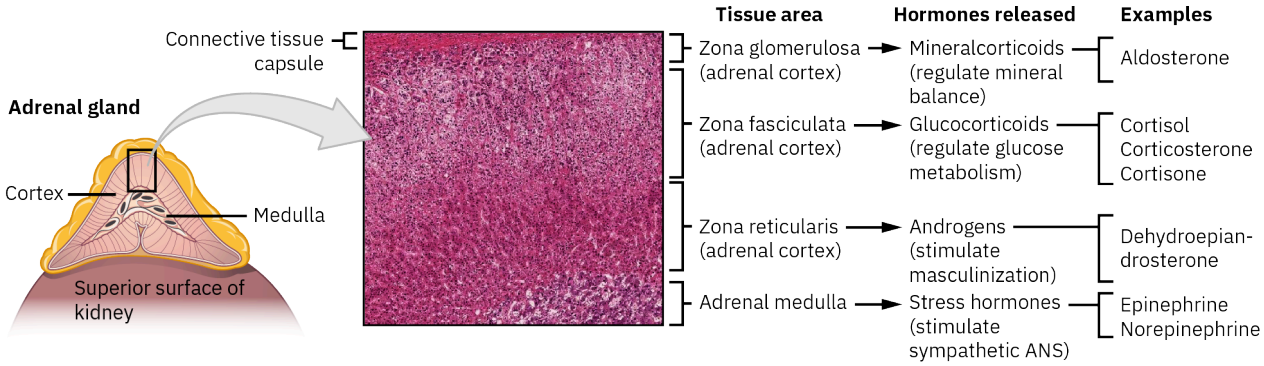


FIGURE 26.4 The adrenal glands produce hormones that are important for regulating body function and the stress response. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Adrenal Cortex Function

The hormones produced by the adrenal cortex regulate various bodily functions. These hormones maintain the body's internal environment by regulating electrolyte, pH, and water balance; glucose metabolism; and immune function. Additionally, the adrenal cortex is involved in responding to stressors because its hormones help the body adapt to physical and emotional stress (Huecker et al., 2023; National Institutes of Health [NIH], 2017).

The adrenal cortex's importance cannot be overstated—it is crucial for maintaining overall health and well-being. Without the hormones from the adrenal cortex, the body would struggle to maintain a stable internal environment, making it vulnerable to various health issues. Therefore, it is essential to maintain the adrenal cortex's health and function to ensure optimal health and wellness (Huecker et al., 2023; NIH, 2017).

LINK TO LEARNING

The Hypothalamic-Pituitary-Adrenal Axis

Access multimedia content (https://openstax.org/books/pharmacology/pages/26-1-introduction-to-the-adrenal-cortex-pituitary-and-hypothalamus)

The Foundation of Neuroscience Open Educational Resources presents information on the stress response. This educational video discusses the hypothalamic-pituitary-adrenal axis (HPA).

The HPA axis is a neuroendocrine system involved in the body's stress response. The hypothalamus releases CRH, which stimulates the pituitary gland to release adrenocorticotropic hormone (ACTH). ACTH then triggers the

adrenal glands to produce cortisol, also known as the stress hormone, which regulates various physiological processes and helps the body cope with stress.

Adrenal Cortex Hormones

Some of the hormones produced by the adrenal cortex include:

- *Mineralocorticoids:* produced in the zona glomerulosa, these help regulate the balance of electrolytes, particularly sodium and potassium, in the body as well as water balance.
- *Glucocorticoids:* produced in the the zona fasciculate, these help regulate metabolism, immune function, and the body's response to stress.
- *Androgens:* produced in the zona reticularis, these contribute to sexual development and fertility in males.

26.2 Growth Hormones and Suppressants

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 26.2.1 Identify the characteristics of growth hormone drugs used to treat pituitary disorders.
- 26.2.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of growth hormone drugs used to treat pituitary disorders.
- 26.2.3 Describe nursing implications of growth hormone drugs used to treat pituitary disorders.
- 26.2.4 Explain the client education related to growth hormone drugs used to treat pituitary disorders.

Growth Hormone

Growth hormones and suppressants are used to treat various growth and development disorders. Growth hormone, also known as somatotropin or human growth hormone, is essential for the body's growth and development. Growth hormone stimulates the production of the insulin-like growth factor-1 (IGF-1) in the liver, which promotes the growth of bone, muscle, and other tissues. Growth hormone also helps to regulate metabolism and break down fats. Growth hormone is particularly important during childhood and adolescence when it promotes the growth and development of the body. However, growth hormone continues to be important throughout adulthood, helping to maintain healthy bone density, muscle mass, and overall well-being.

Deficiencies in growth hormone can lead to stunted growth, delayed puberty, and other health issues. Conversely, excessive growth hormone production can result in abnormal growth of bones and soft tissues, causing gigantism in children or **acromegaly** in adults.

Somatropin

Somatropin (different from somatotropin mentioned above) is a recombinant growth hormone that is used to treat failure to grow due to growth hormone deficiency in pediatric and adult clients; some forms of this prescription are indicated in the treatment of **Prader-Willi syndrome**. The drug is available in a subcutaneous injection dosage form and is individualized based on the client needs.

Drug interactions include glucocorticoids, which may oppose the growth-promoting effects of somatropin; oral estrogen, which impacts growth hormone secretion; and insulin or oral diabetes drugs, which may need dosages altered due to somatropin increasing glucose levels in the blood. The most common adverse effects are injection site reaction, rash, lipoatrophy, thyroid hormone suppression, and headaches. Somatropin is contraindicated in clients who are critically ill or have active malignancy, impaired glucose tolerance or diabetes, hypersensitivity, or closed epiphyses.

Growth Hormone Suppressants

Growth hormone suppressants are medications used to reduce the production or activity of growth hormone in the body. These drugs are typically used to treat medical conditions such as acromegaly or gigantism. Suppressants include somatostatin analogs, dopamine agonists, and growth hormone receptor antagonists. Nurses should note that these drugs should only be used under the guidance of a qualified health care provider because they can have significant side effects on the body and may interact with other medications or medical conditions.

Bromocriptine Mesylate

Bromocriptine mesylate is a dopamine receptor agonist. This grown hormone suppressant stimulates the dopamine receptors in the brain and helps to reduce prolactin production as well as lessen symptoms of Parkinson's disease. It also is used to treat clients with acromegaly or those with high levels of prolactin, which can cause a lack of menstrual periods and infertility. Bromocriptine mesylate is readily absorbed by the gastrointestinal tract and mainly excreted in the urine. Adverse effects include nausea, headache, dizziness, fatigue, vomiting, abdominal cramps, nasal congestion, constipation, and drowsiness. This drug is contraindicated in clients with uncontrolled hypertension, hypersensitivity, and pregnancy.

Lanreotide Acetate

The growth hormone suppressant lanreotide acetate is a somatostatin analog and is used to treat acromegaly in clients who have had an inadequate response to or cannot be treated with surgery and/or radiotherapy and to treat clients with certain types of unresectable tumors. Drug interactions include cyclosporine, bromocriptine, and beta blockers. Adverse reactions include diarrhea, cholelithiasis, abdominal pain, nausea, and injection site reactions. Lanreotide acetate is contraindicated in clients with previous hypersensitivity reaction to lanreotide or any of the ingredients in the formulation.

Octreotide Acetate

Octreotide acetate inhibits growth hormone as a suppressant and is used in the treatment of acromegaly and certain types of tumors. See Table 26.3 for additional information on octreotide acetate.

Pegvisomant

The growth hormone receptor antagonist pegvisomant is indicated for the treatment of acromegaly in clients who have inadequate response to surgery or radiation therapy or for whom these therapies are inappropriate. Adverse reactions include infection, pain, nausea, diarrhea, abnormal liver tests, flu-like symptoms, and injection site reactions. Pegvisomant is contraindicated in clients with diabetes or hypoglycemia, liver toxicity, or hypersensitivity.

Table 26.2 lists common growth hormone suppressants and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Bromocriptine mesylate (Parlodel)	*Acromegaly:* *Adults:* 1.25–2.5 mg orally once daily. May increase by 1.25–2.5 mg every 2–7 days until optimal therapeutic response is achieved. Typical maintenance dose: 20–30 mg/day, in divided doses. Maximum dose: 100 mg/day. *Children:* Not Food and Drug Administration (FDA) approved for children. *Prolactin-secreting pituitary adenoma:* *Adults:* 1.25–2.5 mg orally once daily. May increase every 2–7 days until optimal therapeutic response is achieved. Typical maintenance dose: 2.5–15 mg/day. *Children 11–15 years of age:* Initial dose: One-half to one 2–5 mg scored tablet orally once daily. Dosing may need to be increased as tolerated until a therapeutic response is achieved. Therapeutic dosage: 2.5–10 mg daily.
Lanreotide acetate (Somatuline)	*Acromegaly:* *Adults:* 90 mg subcutaneously every 4 weeks for 3 months; thereafter, dosing is based on growth hormone levels. *Children:* Safety not established in children.

TABLE 26.2 **Drug Emphasis Table: Growth Hormone Suppressants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Octreotide acetate (Sandostatin)	*Acromegaly:* *Adults:* Initial dose: 50 mcg subcutaneously, 2–3 times daily; no added benefit from doses beyond 300 mcg/day. Other routes of administration include intramuscular (depot) and oral. *Children:* Safety not established in children.
Pegvisomant (Somavert)	*Acromegaly:* *Adults:* Loading dose: 40 mg subcutaneously; on the following day, begin 10 mg subcutaneously daily. Adjust in 5 mg increments every 4–6 weeks based on serum IGF-1 concentrations. Recommended dosage: 10–30 mg/day subcutaneously; maximum dose: 30 mg/day. *Children:* Safety not established in children.

TABLE 26.2 **Drug Emphasis Table: Growth Hormone Suppressants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects of growth hormone suppressants include gastrointestinal symptoms such as abdominal pain, diarrhea, nausea, and vomiting; low or high blood glucose levels; vitamin B_{12} deficiency; fatigue and weakness; and injection site reactions such as redness, swelling, and pain at the injection site.

Contraindications include hypersensitivity to the drugs or any of their components, uncontrolled diabetes—as growth hormone suppressants can have potential effects on blood glucose regulation—severe liver disease, and severe kidney disease. These drugs are metabolized by the liver and can cause further hepatic impairment in clients with liver disease, and because they are excreted in the urine, they can cause further renal insufficiency in clients with kidney disease.

Table 26.3 is a drug prototype table for growth hormone suppressants featuring octreotide acetate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Growth hormone suppressant **Mechanism of Action** Exerts pharmacologic actions similar to the natural hormone somatostatin and inhibits growth hormone, glucagon, and insulin	**Drug Dosage** *Adults:* Initial dose: 50 mcg subcutaneously, 2–3 times daily; no added benefit from doses beyond 300 mcg/day. Other routes of administration include intramuscular (depot) and oral. *Children:* Safety not established in children.
Indications Acromegaly Carcinoid tumors Vasoactive intestinal peptide tumors **Therapeutic Effects** Reduces growth hormone Reduces tumor size or and improves symptoms of carcinoid tumors	**Drug Interactions** Beta blockers Insulin Oral diabetes drugs **Food Interactions** No significant interactions
Adverse Effects Gall bladder abnormalities Bradycardia and arrhythmias Diarrhea/nausea/abdominal discomfort Hypo/hyperglycemia Hypothyroidism	**Contraindications** Hypersensitivity Atrioventricular block Caution: Monitor closely in clients who have cholelithiasis or complications of cholelithiasis

TABLE 26.3 **Drug Prototype Table: Octreotide Acetate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking growth hormone suppressants:

- Assess the client's medical history, current drug list, and allergies.
- Assess the client's baseline height, weight, and vital signs.
- Ensure the drug is prepared appropriately using aseptic technique and verify dosage before administration.
- Monitor the client's response to the drug, including any changes in height, weight, and vital signs.
- Monitor closely for injection site reactions and other adverse reactions such as pain, nausea, and diarrhea.
- Monitor IGF-1 levels and liver function, and report abnormalities to the health care provider.
- Monitor for thyroid suppression and elevated glucose levels and notify the health care provider of abnormalities.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a growth hormone suppressant should:

- Keep this drug in its original carton to protect it from light.
- If injectable:
  - Choose injection site (thigh, abdomen, or buttock) as recommended by their health care provider, avoiding areas that are bony, bruised, sore, red, scarred, or hard.
  - Cleanse injection area with an alcohol swab/pad and let dry for 30 seconds before administering the drug.
  - Dispose of needles in an FDA-approved sharps disposal container after use.
- Keep a journal of their symptoms and note improved or worsening symptoms.
- Report symptoms of fluid retention, including swelling in legs and feet, weight gain, and shortness of breath, or other symptoms such as constipation, fatigue, dry skin, increased thirst, polyuria, blurred vision, muscle pain, and/or tingling in hands and feet to their health care provider because these may represent an adverse reaction to the drug.
- Speak to their health care provider if they are pregnant or plan on becoming pregnant before starting these drugs because they can impact the fetus.
- Store out of reach from children and away from heat, moisture, and light.

The client taking a growth hormone suppressant *should not:*

- Dispose of needles or sharps container in the household trash.
- Reuse needles.
- Stop taking the drug unless directed by the health care provider because this drug class replaces or suppresses the body's growth hormone.

26.3 Antidiuretic Hormones

Antidiuretic Hormones

Learning Outcomes

By the end of this section, you should be able to:

- 26.3.1 Identify the characteristics of ADH drugs used to treat pituitary disorders.
- 26.3.2 Explain the indications, actions, adverse reactions, and interactions of ADH drugs used to treat pituitary disorders.
- 26.3.3 Describe nursing implications of ADH drugs used to treat pituitary disorders.
- 26.3.4 Explain the client education related to ADH drugs used to treat pituitary disorders.

ADH is produced in the hypothalamus and released by the pituitary. This hormone plays a crucial role in regulating fluid balance in the body and maintaining normal physiologic function. ADH reduces the amount of urine produced

by the kidneys by causing the renal tubules to increase water reabsorption, which reduces the amount of urine produced and helps to maintain the body's fluid balance. When ADH is released, it causes the kidneys to retain water, which leads to an increase in blood volume and a decrease in urine output.

In conditions where there is a deficiency or dysfunction of ADH, such as **diabetes insipidus**, excessive urine output can occur, leading to dehydration, electrolyte imbalances, and manifestations of polydipsia and hypotonic polyuria (Christ-Crain & Gaisl, 2021). Conversely, an excess of ADH production can cause water retention and low sodium levels as with **syndrome of inappropriate antidiuretic hormone (SIADH)**. Excess ADH can result in manifestations of symptomatic hyponatremia, such as muscle cramps, nausea, and vomiting (Mentrasti et al., 2020; Yasir & Mechanic, 2023).

Desmopressin Acetate

Desmopressin acetate is a synthetic ADH that regulates water balance and blood pressure by promoting water retention in the kidneys and reducing the amount of urine produced. It also increases clotting factor levels in the blood. Desmopressin is commonly used to treat diabetes insipidus, nocturnal enuresis (bed wetting), and bleeding disorders such as hemophilia A. Adverse effects include headache, nausea, and low sodium levels. It is contraindicated in clients with severe renal impairment, a history of hyponatremia, or hypersensitivity.

Vasopressin

Vasopressin, also known as antidiuretic hormone, is released by the posterior pituitary gland. Its primary function is to regulate water balance in the body by controlling the amount of water excreted in the urine. This hormone binds to vasopressin receptors in the cells of the kidneys, which increases the reabsorption of water back into the bloodstream. The reabsorption helps reduce the amount of water lost in the urine and can prevent dehydration. Vasopressin also has vasoconstrictor effects, causing narrowing of blood vessels and an increase in blood pressure, making it useful as a drug to treat conditions such as shock or cardiac arrest.

Demeclocycline

Demeclocycline is a tetracycline antibiotic that is rarely used for its antibiotic properties. This drug interferes with vasopressin and is used to treat SIADH. It helps to regulate water balance, leading to an increase in urine output and a reduction in the amount of water in the body. Adverse effects include nausea, vomiting, diarrhea, and photosensitivity. Demeclocycline is contraindicated in clients with hypersensitivity.

Tolvaptan

Tolvaptan is used to treat a condition called hyponatremia (low serum sodium levels). This drug works by blocking the action of vasopressin, which helps the body to retain water and maintain electrolyte homeostasis, and is used to treat conditions such as SIADH, heart failure, liver disease, and kidney disease. Tolvaptan should be initiated and re-initiated in a hospital setting where serum sodium levels can be monitored closely. A too rapid correction of hyponatremia can cause osmotic demyelination, resulting in seizures, coma, and death. Adverse effects include dry mouth, constipation, thirst, hyperglycemia, and polyuria. It is contraindicated in clients with hypovolemic hyponatremia or hypersensitivity.

Table 26.4 lists common antidiuretic hormones and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Desmopressin (DDAVP, Stimate)	Individualized based on condition being treated and severity of symptoms. Typical dose: 2–4 mcg orally in 1–2 daily doses. Close monitoring is recommended.
Vasopressin (ADH, Vasostrict)	Individualized based on condition being treated and severity of symptoms. *For diabetes insipidus (injectable):* Recommended starting dose: 2–4 mcg in 1–2 divided doses subcutaneously or intravenously. The morning and evening doses should be separately adjusted for an adequate diurnal rhythm of water turnover. Adjust dose based on response to treatment, estimated by two parameters: adequate duration of sleep and adequate, not excessive, water turnover. *For diabetes insipidus (intranasal):* Recommended dose: 10 mcg once daily into one nostril up to 40 mcg once daily (or 40 mcg divided into 2–3 daily doses). If administered more than once a day, adjust for an adequate diurnal rhythm of urine output. *For shock (diluted):* 0.01–0.03 units/minute intravenously, titrated every hour.
Demeclocycline (Declomycin)	4 divided doses of 150 mg each or 2 divided doses of 300 mg each orally daily. Maximum dose: 600 mg/day.
Tolvaptan (Jynarque, Samsca)	15–30 mg orally daily. Maximum dose: 60 mg/day.

TABLE 26.4 **Drug Emphasis Table: ADHs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Typical adverse effects of ADH drug classification include fluid retention and hyponatremia—by reducing urine output, which can lead to fluid retention and low sodium levels—headache, and gastrointestinal symptoms such as abdominal cramps, nausea, and vomiting.

Contraindications include hyponatremia, cardiovascular disease, and kidney disease. Using ADH drugs may exacerbate or worsen hyponatremia. With cardiovascular disease, ADH drugs can cause vasoconstriction, which can worsen angina, elevate blood pressure, and promote fluid retention that can exacerbate heart failure and lead to fluid volume overload. Nurses should note that these drugs are excreted in the urine and can further impair renal function of clients with kidney disease.

Table 26.5 is a drug prototype table for ADHs featuring vasopressin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antidiuretic hormone **Mechanism of Action** Binds to vasopressin receptors in the cells of the kidneys, which increases reabsorption of water back into the bloodstream, helping to reduce the amount of water lost in urine and helping prevent dehydration	**Drug Dosage** Individualized based on condition being treated and severity of symptoms. *For diabetes insipidus (injectable):* Recommended starting dose: 2–4 mcg in 1–2 divided doses subcutaneously or intravenously. The morning and evening doses should be separately adjusted for an adequate diurnal rhythm of water turnover. Adjust dose based on response to treatment, estimated by two parameters: adequate duration of sleep and adequate, not excessive, water turnover. *For diabetes insipidus (intranasal):* Recommended dose: 10 mcg once daily into one nostril up to 40 mcg once daily (or 40 mcg divided into 2–3 daily doses). If administered more than once a day, adjust for an adequate diurnal rhythm of urine output. *For shock (diluted):* 0.01–0.03 units/minute intravenously, titrated every hour.
Indications Vasodilatory shock **Therapeutic Effects** Increases blood pressure	**Drug Interactions** Catecholamines Indomethacin Ganglionic blocking agents Antidepressants Lithium **Food Interactions** No significant interactions
Adverse Effects Bradycardia Increased bilirubin levels Hyponatremia Ischemic lesions Decreased platelets	**Contraindications** Hypersensitivity Caution: Monitor closely when administering to clients with impaired cardiac response

TABLE 26.5 **Drug Prototype Table: Vasopressin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ADHs:

- Educate the client regarding ADH drugs.
- Assess the client's knowledge about signs and symptoms of over- and undertreatment, adverse reactions, and contraindications and clarify any gaps in knowledge.
- Monitor client fluid intake and urine output closely.
- Monitor electrolytes, especially sodium, as well as urine specific gravity.
- Monitor client and report any abnormalities or symptoms of water intoxication and fluid excess such as nausea, vomiting, headache, changes in mental status, muscle cramps, and drowsiness or fluid loss such as extreme thirst, dry mouth, and feelings of tiredness or fatigue.
- Monitor nasal passages for ulceration if administering via nasal route.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antidiuretic hormone should:

- Keep a journal of their symptoms. It may take several weeks for them to notice improved symptoms.
- Report symptoms of irregular nausea, vomiting, headache, changes in mental status, muscle cramps, drowsiness, extreme thirst, dry mouth, and feelings of tiredness or fatigue to their health care provider because these may represent an adverse reaction to the drug.
- Monitor their fluid intake and urine output.

The client taking an antidiuretic hormone *should not:*

- Stop taking the drug unless directed by their health care provider.

FDA BLACK BOX WARNING

Antidiuretic Hormones

Desmopressin acetate may precipitate hyponatremia, which may be life-threatening if severe.

Tolvaptan can cause serious and potentially fatal liver injury. Tolvaptan should be initiated and re-initiated only in a hospital where serum sodium levels can be monitored closely. A too rapid correction of hyponatremia can cause osmotic demyelination resulting in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma, and death.

26.4 Glucocorticoids and Mineralocorticoids

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 26.4.1 Identify the characteristics of glucocorticoid and mineralocorticoid drugs used to treat adrenal disorders.
- 26.4.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of glucocorticoid and mineralocorticoid drugs used to treat adrenal disorders.
- 26.4.3 Describe nursing implications of glucocorticoid and mineralocorticoid drugs used to treat adrenal disorders.
- 26.4.4 Explain the client education related to glucocorticoid and mineralocorticoid drugs used to treat adrenal disorders.

Glucocorticoids

Glucocorticoids and mineralocorticoids are two types of steroid hormones that are produced by the adrenal cortex and play distinct roles in regulating the body's metabolism, fluid balance, and stress response. **Glucocorticoids** are produced in response to stress and help regulate metabolism and the immune system.

The primary glucocorticoid in the body is **cortisol**. Cortisol helps regulate glucose uptake in other tissues—such as muscles and fat—and has an anti-inflammatory and immunosuppressive effect, making it an important medication in the treatment of many inflammatory and autoimmune disorders and in preventing transplantation rejection. Nurses should note that there are many corticosteroids within this class of drugs, and they vary by potency, route of administration, and other non-anti-inflammatory activity. These properties help the health care provider choose the appropriate corticosteroid agent to prescribe for the client. Synthetic glucocorticoids—such as prednisone, dexamethasone, and hydrocortisone—are commonly used in medicine to treat conditions such as asthma, rheumatoid arthritis, and inflammatory bowel disease.

Although glucocorticoids can be effective at treating certain conditions, they can have significant toxic effects over time that limit use. As such, their use is typically reserved for short-term treatment of acute conditions or as a last resort for long-term conditions that have not responded to other treatments. Short-term use is tapered quickly to avoid rebound symptoms. Long-term use also requires tapering due to HPA axis suppression resulting in inadequate cortisol production.

Cortisone Acetate

Cortisone acetate is a glucocorticoid that also has salt-retaining properties. It is indicated for use with primary or secondary adrenocortical insufficiency, hypercalcemia associated with cancer, rheumatic disorders, collagen disorders, allergic states, inflammatory bowel disorders, and various respiratory, hematologic, integumentary, and neoplastic disorders. Adverse effects include fluid retention, sodium retention, hypertension, muscle weakness, osteoporosis, headache, and weight gain.

Hydrocortisone

Hydrocortisone, a synthetic form of cortisol, is a short-acting glucocorticoid that is used to reduce inflammation and swelling in the body. Hydrocortisone is used to treat a variety of conditions including skin disorders, allergic reactions, asthma, arthritis, and certain types of cancer. It can be applied topically, as a cream or ointment, and has ophthalmic, otic, and rectal routes available. Adverse effects include headache, dizziness, nausea, weight gain, mood changes, increased blood pressure, hyperglycemia, difficulty sleeping, dry skin, acne, skin irritation, and increased risk of infections.

CLINICAL TIP

Hydrocortisone Administration

Systemic administration of steroids is often recommended to take place in the morning to avoid insomnia (Hodgens & Sharman, 2023).

Methylprednisolone

Methylprednisolone is an intermediate-acting synthetic glucocorticoid that is used as an anti-inflammatory and immunosuppressant. It is commonly used to treat a variety of inflammatory and autoimmune conditions. Methylprednisolone—available in oral, injectable, and topical forms—works by binding to glucocorticoid receptors in the cells of the body, which leads to a reduction in the release of inflammatory molecules, such as cytokines, and inhibits the immune response and decreases inflammation. Dosing is based on the condition being treated and the severity of symptoms.

Prednisolone

Prednisolone, an intermediate-acting synthetic form of cortisol, is used to decrease inflammation and to treat a variety of conditions including rheumatic conditions, allergic reactions, asthma, and certain types of cancer. The medication comes in an oral form and as an injectable. Adverse effects include increased glucose levels, injection site reactions, weight gain, and mood changes.

Prednisone

Prednisone is an intermediate-acting steroid medication and a synthetic form of cortisol used to reduce inflammation. Like prednisolone, it is used in the treatment of a variety of conditions including asthma, allergic reactions, rheumatic disorders, respiratory disorders, and certain types of cancer. Adverse effects include weight gain, mood changes, increased blood sugar levels, and osteoporosis.

Betamethasone

Betamethasone is a long-acting synthetic cortisol that reduces inflammation and swelling in the body and is used to treat various disorders including skin and inflammatory disorders such as rheumatoid arthritis. Adverse effects include skin irritation, increased risk of infection, and elevated blood glucose levels.

Dexamethasone

Dexamethasone is a long-acting synthetic form of cortisol that is used to reduce inflammation in the body and may also be used as an immunosuppressant. Dexamethasone, which comes in an oral and injectable form, is used to treat numerous disorders including rheumatic, respiratory, asthma, and allergic reactions. This drug is also used in the diagnosis of Cushing's syndrome as a suppressive test. Adverse effects include increased risk of infection, weight gain, irritability and mood changes, increased blood sugar levels, GI upset, and osteoporosis.

Table 26.6 lists common glucocorticoids and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Cortisone acetate (Cortison, Cortisyl)	*Typical dose*: 25–300 mg orally daily depending on the specific disease entity being treated.
Hydrocortisone (Cortisporin, Cortizone, Solu-Cortef, Proctocort)	*Topical cream:* Depends on formulation, typically 1%, 3–4 times daily. *IV:* 100–500 mg; dose extremely variable based on client and indication.
Methylprednisolone (Medrol, Solu-Medrol)	*Typical dose*: 4–200 mg daily depending on the specific disease entity being treated. Routes include oral (dose-pack, tablets, solution), intravenous, intra-articular, and intramuscular.
Prednisolone (Millipred, Omnipred, Prelone)	*Typical dose*: 5–60 mg orally daily depending on the specific disease entity being treated.
Prednisone (Deltasone)	*Typical dose*: 5–60 mg orally daily depending on the specific disease entity being treated.
Betamethasone (Celestone, Betaject)	*Typical dose for injectable*: 0.25–0.9 mg/day intravenously or intramuscularly.
Dexamethasone (Decadron, Dexasone)	*Typical dose*: 0.5–9 mg daily depending on the specific disease entity being treated. Routes include oral, intravenous, intra-articular, and intramuscular.

TABLE 26.6 **Drug Emphasis Table: Glucocorticoids** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Short-term adverse effects include insomnia, hunger, and mood changes. Long-term adverse effects include weight gain, high blood pressure, osteoporosis, hyperglycemia, skin atrophy (topical application), iatrogenic **Cushing's syndrome**, and increased risk of infection.

Glucocorticoids are contraindicated in clients with hypersensitivity to any component of the formulation, those who have an active systemic fungal infection, or those with uncontrolled hyperglycemia.

Table 26.7 is a drug prototype table for glucocorticoids featuring methylprednisolone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Synthetic glucocorticoid **Mechanism of Action** Binds to glucocorticoid receptors, decreasing the release of inflammatory molecules and inhibiting the immune response	**Drug Dosage** *Typical dose:* 4–200 mg daily depending on the specific disease entity being treated. Routes include oral (dose-pack, tablets, solution), intravenous, intra-articular, and intramuscular.
Indications Inflammatory conditions Autoimmune disorders **Therapeutic Effects** Decreases inflammation Suppresses the immune response	**Drug Interactions** Oral anticoagulants Aspirin **Food Interactions** No significant interactions
Adverse Effects Weight gain High blood pressure Osteoporosis Increased risk of infection Skin atrophy Hyperglycemia/glycosuria	**Contraindications** Hypersensitivity Systemic active fungal infections Caution: May increase risk of infection

TABLE 26.7 **Drug Prototype Table: Methylprednisolone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Mineralocorticoids

Mineralocorticoids are a type of steroid hormones that are produced by the adrenal cortex and are involved in regulating the body's fluid balance and electrolyte levels. The primary mineralocorticoid in the body is aldosterone.

Disorders of mineralocorticoid production or activity can lead to imbalances in fluid and electrolyte levels: two such conditions exist. The first is hyperaldosteronism, which is characterized by excess aldosterone production. An excess of aldosterone causes an increase in blood pressure and serum sodium levels along with a decrease in serum potassium levels. The other condition is hypoaldosteronism, which is characterized by insufficient aldosterone production. Hypoaldosteronism leads to a decrease in blood pressure and serum sodium levels along with an increase in serum potassium levels.

Aldosterone

Aldosterone works by binding to mineralocorticoid receptors in the cells of the kidneys, which increases the reabsorption of sodium ions and the excretion of potassium ions. This leads to an increase in blood volume and blood pressure. In addition to regulating fluid and electrolyte balance, aldosterone plays a role in the **renin-angiotensin-aldosterone system (RAAS)**. The RAAS is a complex hormonal system that helps to regulate blood pressure by controlling the balance of sodium and water in the body.

Fludrocortisone

Fludrocortisone is a synthetic adrenocortical steroid that binds to mineralocorticoid receptors in the cells of the kidneys and supports fluid and electrolyte balance within the body. This medication is used to treat primary and secondary adrenocortical insufficiency in **Addison's disease**. Adverse effects include hyperglycemia, hypokalemia, hypertension, muscle weakness, and impaired wound healing. It is contraindicated in clients with fungal infections and hypersensitivity.

Adverse Effects and Contraindications

Common adverse effects of mineralocorticoid drugs include fluid retention because they promote sodium and water reabsorption in the kidneys; hypokalemia where symptoms include muscle weakness, fatigue, irregular heartbeat, and muscle cramps; elevated blood pressure; gastrointestinal disturbances such as stomach discomfort, nausea, and diarrhea; and mood and behavioral changes such as mood swings, irritability, or anxiety.

Contraindications include hypersensitivity to the drug or any of its components, systemic fungal infections, heart

failure, and severe kidney impairment. Mineralocorticoids can suppress the immune system and worsen systemic fungal infections; heart failure is contraindicated because these drugs can cause fluid retention and lead to worsening of fluid volume overload; and severe kidney impairment can occur in clients with kidney disease as these drugs are excreted through the urine and can cause further renal insufficiency.

Table 26.8 is a drug prototype table for mineralocorticoids featuring fludrocortisone acetate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Mineralocorticoid **Mechanism of Action** Binds to mineralocorticoid receptors in the cells of the kidneys, which increases the reabsorption of sodium ions and the excretion of potassium ions, helping to regulate fluid and electrolyte balance	**Drug Dosage** *For salt-losing adrenogenital syndrome:* Typical dose: 0.1–0.2 mg orally daily. *For Addison's disease:* Usual dose: 0.1 mg orally daily, although dosage ranging from 0.1 mg 3 times a week to 0.2 mg daily has been employed.
Indications Primary and secondary adrenocortical insufficiency in Addison's disease Treatment of salt-losing adrenogenital syndrome **Therapeutic Effects** Generalized extracellular fluid volume expansion	**Drug Interactions** Amphotericin B Potassium-depleting diuretics Digitalis glycosides Oral anticoagulants Antidiabetic drugs Aspirin Barbiturates Phenytoin Rifampin Anabolic steroids Vaccines Estrogen **Food Interactions** No significant interactions
Adverse Effects Edema Cardiac enlargement Potassium loss Muscle weakness Abdominal distention Impaired wound healing Growth suppression Hyperglycemia Urticaria	**Contraindications** Systemic fungal infections Hypersensitivity Caution: May mask infections

TABLE 26.8 **Drug Prototype Table: Fludrocortisone Acetate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking glucocorticoids and mineralocorticoids:

- Educate the client regarding glucocorticoid and mineralocorticoid therapy.
- Assess the client's knowledge about signs and symptoms of over- and undertreatment, adverse reactions, and contraindications and clarify any gaps in knowledge.
- Monitor vital signs and electrolytes, especially sodium and potassium, renal function, glucose levels, serum aldosterone levels, serum cortisol levels, and bone density test, closely.
- Report any abnormalities or symptoms such as weight gain, edema, crackles, jugular vein distention, fever,

tachycardia, tachypnea, shortness of breath, or a change in mental status to the health care provider.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a glucocorticoid or mineralocorticoid should:

- Take drugs as prescribed by their health care provider.
- If using the drug systemically, avoid people who are sick—especially those who have chickenpox, measles, or tuberculosis—because they are at an increased risk of contracting the condition.
- Report signs of fluid volume overload such as a weight gain of 2 pounds in 3 days or 5 pounds in a week.
- Limit salt intake.
- Report symptoms of infection, such as a fever greater than 100.4°F, a fast heartbeat, fast breathing, and symptoms of electrolyte imbalances such as weight gain, edema, a change in mental status, or shortness of breath and symptoms of cardiovascular issues including jugular vein distention, tachycardia, and/or palpitations to the health care provider.

The client taking a glucocorticoid or mineralocorticoid *should not:*

- Stop taking this medication without consulting with the health care provider because this drug must be tapered to decrease adverse effects.

FDA BLACK BOX WARNING

Corticosteroids

Injection into the epidural space of the spine may result in rare but serious adverse events including loss of vision, stroke, paralysis, and death.

Chapter Summary

This chapter provided an overview of the hypothalamus, pituitary gland, and adrenal cortex, which are essential components of the endocrine system. The hypothalamus is a small region of the brain that plays a key role in the regulation of many physiological processes in the body including hunger, thirst, and body temperature. It is also responsible for the regulation and release of pituitary hormones from the pituitary gland, which is sometimes referred to as the "master gland" because it controls the release of hormones from other endocrine glands. The adrenal cortex, part of the adrenal gland, is responsible for regulating fluid and electrolyte balance, glucose metabolism, adaptation to stress, and immune function.

This chapter covered drugs that are commonly used to treat conditions related to the hypothalamus, pituitary, and adrenal cortex. Overall, the hypothalamus, pituitary, and adrenal cortex play critical roles in the regulation of many physiological processes in the body. Disorders affecting the function of these structures can have significant impacts on health and well-being.

Key Terms

acromegaly an abnormal growth caused by overproduction of the growth hormone by the pituitary gland

Addison's disease a long-term condition in which the adrenal glands do not produce enough cortisol and aldosterone

adenohypophysis anterior pituitary gland

adrenal cortex the outer portion of the adrenal glands that produce hormones, which support vital body functions

adrenal glands a small gland at the top of each kidney that produces steroid hormones, adrenaline, and noradrenaline

antidiuretic hormone (ADH) a chemical produced in the brain that causes kidneys to release less water

cortisol the hormone produced by the two adrenal glands that plays an important role in stress response

Cushing's syndrome a condition in which the body overproduces the hormone cortisol

diabetes insipidus a disease in which the secretion of or response to vasopressin is impaired, resulting in the production of large quantities of hypotonic urine

endocrine system a messenger system of glands and organs that produce and release hormones to maintain homeostasis within the body

glucocorticoids a group of steroids involved in carbohydrate, protein, and fat metabolism that has anti-inflammatory properties

homeostasis a state of balance

hypophysis the pituitary gland

hypothalamus a region in the forebrain that coordinates the autonomic nervous system and pituitary gland activity

mineralocorticoids steroids that are involved in maintaining fluid, sodium, and potassium balance within the body

neuroendocrine system the communication system between the nervous and endocrine systems

neurohypophysis the posterior pituitary gland

pituitary gland a pea-sized gland located at the base of the brain that is part of the endocrine system, also known as the master gland

Prader-Willi syndrome a genetic disorder resulting in physical, mental, and behavioral problems

renin-angiotensin-aldosterone system (RAAS) a hormone system that regulates fluid and electrolyte balance, blood pressure, and systemic vascular resistance

syndrome of inappropriate antidiuretic hormone secretion (SIADH) occurs when excessive levels of antidiuretic hormones are produced

vasopressin a nonapeptide synthesized by the hypothalamus and stored in the posterior pituitary, also known as ADH or human vasopressin, which helps to regulate fluid volume

zona fasciculate the middle layer of the adrenal cortex

zona glomerulosa the outermost layer of the adrenal cortex

zona reticularis the innermost layer of the adrenal cortex

Review Questions

1. A client is diagnosed with a hypothalamic disorder affecting the production of vasopressin. Which of the following manifestations is the nurse least likely to assess in this client?

a. Hypoglycemia

b. Polydipsia
c. Polyphagia
d. Polyuria

2. A client is prescribed a drug that inhibits the action of CRH. After administration of this drug, what should the nurse monitor?
a. TSH
b. Cortisol
c. Estrogen
d. Testosterone

3. A client is prescribed octreotide 150 mcg subcutaneously daily in three divided doses. The available drug comes in a concentration of 100 mcg/mL. How many milliliters should the nurse administer for each dose?
a. 0.5 mL
b. 1.0 mL
c. 1.5 mL
d. 2.0 mL

4. A client with adrenal insufficiency is prescribed hydrocortisone. Which action should the nurse take to detect potential adverse effects of this drug?
a. Monitor for hypoglycemia and hypertension
b. Assess for hyperglycemia and hypertension
c. Check for hypoglycemia and weight loss
d. Assess for weight loss and hypertension

5. A nurse is caring for a client with acromegaly. Which explanation of this disorder will the nurse give to the client?
a. "Excess growth hormone causes increased bone density."
b. "Increased growth hormone results in decreased insulin resistance."
c. "Elevated growth hormone leads to increased muscle mass and strength."
d. "Too much growth hormone causes abnormal growth of bones and soft tissues."

6. A client is prescribed fludrocortisone. Which findings indicate to the nurse that the client is having adverse effects from this medication?
a. Hypokalemia and hypertension
b. Hypoglycemia and hypertension
c. Hypokalemia and hypotension
d. Hyperglycemia and hypotension

7. A client requires 120 mg of methylprednisolone. The available medication comes in a 125 mg/2 mL vial. How many milliliters should the nurse administer if rounded to the nearest tenth?
a. 1.9 mL
b. 1.8 mL
c. 2.0 mL
d. 2.1 mL

8. A client is being discharged on a glucocorticosteroid drug for a flare-up of rheumatoid arthritis. Which instruction should the nurse give to the client?
a. Stop the medication when symptoms subside.
b. Taper the medication as directed.
c. Take the medication, as needed, for joint pain.
d. Increase the dose each day until pain is relieved.

9. A client with Parkinson's disease has an order for bromocriptine. Which assessment finding would cause the nurse to not administer the drug and notify the provider?
   a. Hypervigilance
   b. Diarrhea
   c. Heart rate 90 beats/minute
   d. Blood pressure 196/108 mm Hg

10. A client presents with hyperaldosteronism. What assessment findings should the nurse expect?
   a. Decreased blood pressure, increased potassium levels
   b. Increased blood pressure, decreased potassium levels
   c. Increased blood pressure, increased potassium levels
   d. Decreased blood pressure, decreased potassium levels

CHAPTER 27
Thyroid and Parathyroid Disorder Drugs

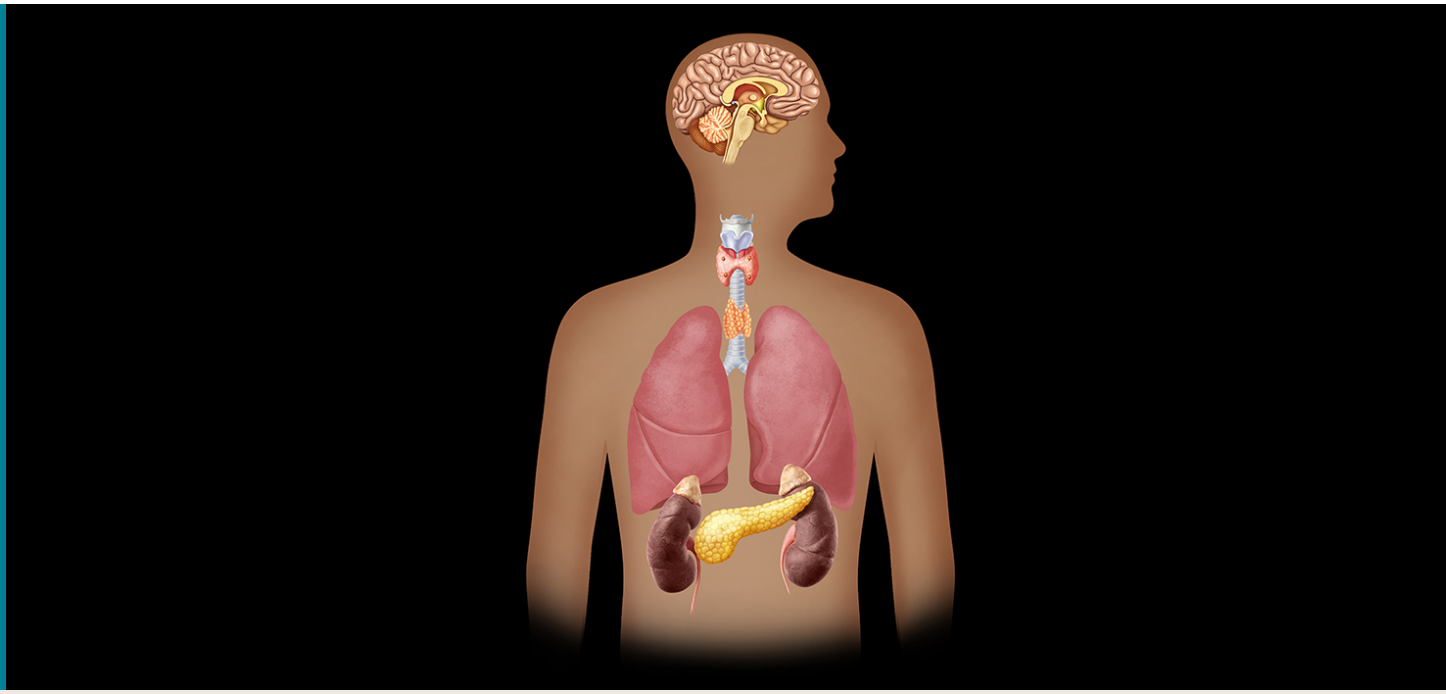


FIGURE 27.1 The endocrine system regulates all biological processes related to development of the brain and nervous system, reproduction, growth, and metabolism. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The endocrine system influences almost every cell in the body. Several organs and glands comprise the endocrine system, which acts as a messenger system within the body. **Endocrine glands** release chemicals called hormones directly into the bloodstream. These hormones control processes that occur within the body. Endocrine hormones help to coordinate bodily functions such as emotions, growth, metabolism, mood, sexual function, and sleep. This chapter will introduce and focus on the thyroid and parathyroid glands.

27.1 Introduction to the Thyroid and Parathyroid

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 27.1.1 Describe the function of the thyroid and parathyroid glands.
- 27.1.2 Discuss hormones associated with the thyroid and parathyroid glands.

Thyroid and Parathyroid Glands

The **thyroid gland** is a butterfly-shaped gland located at the front of the neck below the voice box (see Figure 27.2). This important gland regulates metabolism in the body through the production and secretion of thyroid hormones, which require iodine for synthesis. The thyroid gland produces the active thyroid hormone, **triiodothyronine (T3)**, and the inactive thyroid hormone, **thyroxine (T4)**. Thyroid follicular cells secrete T3 and T4, while parafollicular cells secrete **calcitonin** cells that aid calcium metabolism. Follicular cells line the follicles, which are small spherical structures in the thyroid gland. They absorb iodine from the blood and combine it with T3 and T4. Parafollicular cells

are scattered between the follicles of the thyroid gland. Their main function is to secrete calcitonin for calcium regulation. Calcitonin lowers the levels of calcium in the blood by inhibiting the activity of osteoclasts—cells that break down bone tissue and release calcium into the blood. When calcium levels in the blood rise, the thyroid gland releases calcitonin, which binds to receptors on the surface of osteoclasts and inhibits their activity, reducing the amount of calcium released from the bone into the blood, thereby lowering calcium levels in the blood (McLaughlin & Jialal, 2022).

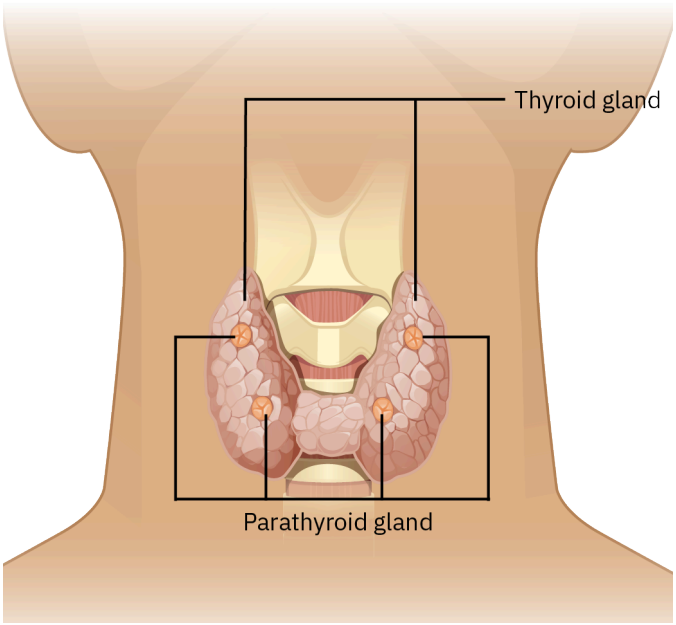


FIGURE 27.2 The thyroid and parathyroid play an important role in body functioning and metabolism. (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Thyroid hormones affect multiple body systems:

- the cardiac system—they have a positive inotropic effect on cardiac output and stroke volume;
- metabolism—they play an important role through heat production and oxygen consumption;
- the respiratory system—they help by normalizing arterial oxygen;
- the nervous system—they stimulate the peripheral nervous system; and
- the reproductive system—they are necessary for growth and development.

The parathyroid glands are four tiny glands that are located on the upper and lower parts of the sides of the thyroid gland (see Figure 27.2). The parathyroid glands secrete **parathyroid hormone (PTH)**, which along with **dihydroxy-vitamin D_3** (vitamin D_3) and calcitonin are responsible for calcium homeostasis within the body. The major target organs for PTH are the kidneys, skeletal system, and intestines. The primary responses to PTH by the kidneys are to increase renal calcium reabsorption and phosphate excretion as well as to enhance the kidney's ability to activate vitamin D so that more calcium is absorbed through the intestine. In addition, it increases the activity of osteoclasts, thereby increasing the resorption of bone (Lofrese et al., 2022; Khan et al., 2022).

When thyroid hormone levels are insufficient within the body, a series of responses is initiated. The process begins with the hypothalamus releasing thyrotropin-releasing hormone (TRH). This hormone acts as a communicator by interacting with the anterior pituitary gland, a small pea-sized gland located at the brain's base. In response to TRH, the anterior pituitary gland releases thyrotropin, also known as **thyroid-stimulating hormone** (TSH). TSH stimulates the thyroid gland, prompting it to either increase or decrease the production of both T4 and T3, essential thyroid hormones.

Conversely, in cases where an excess of thyroid hormones is present, a crucial negative feedback system comes into play. Excessive levels of T4 and T3 instruct the anterior pituitary and hypothalamus to restrain the release of their respective hormones. This control mechanism is of paramount importance in maintaining a balanced hormonal environment. The influence of thyroid hormones extends beyond their impact on metabolism and energy regulation.

These hormones also interact with the parathyroid glands. The secretion of calcitonin, for instance, directly interacts with calcium ions and affects parathyroid hormones. Calcitonin, functioning as an antagonist to the parathyroid gland, contributes to the intricate balance of calcium in the body. Figure 27.3 illustrates thyroid hormones that control metabolism and parathyroid hormones that control calcium homeostasis.

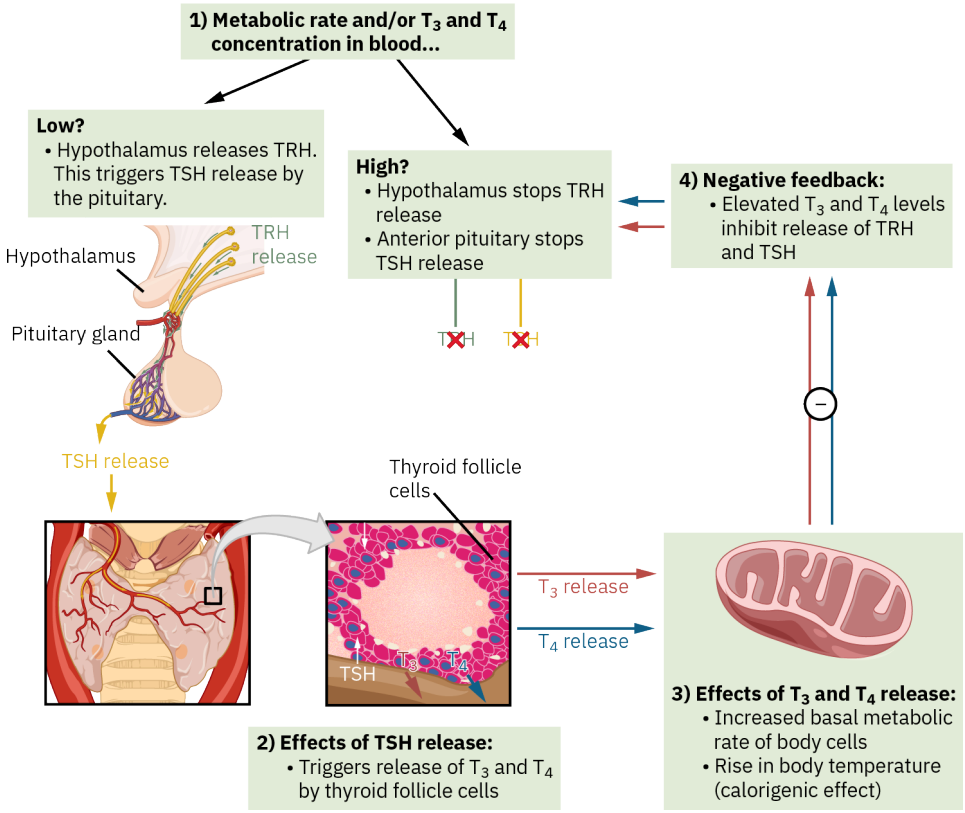


FIGURE 27.3 Thyroid hormones control metabolism and impact parathyroid hormones that control calcium homeostasis within the body. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Hypothyroidism

Hypothyroidism arises from an inadequate secretion of T3 and T4 into the bloodstream, prompting the pituitary gland to release TSH. This dynamic is part of the hypothalamus-pituitary axis, in which the hypothalamus triggers the release of TRH to stimulate the anterior pituitary in the secretion of TSH. **Hashimoto thyroiditis** is the most common cause of hypothyroidism. This condition is caused by an autoimmune-mediated destruction of the thyroid gland, which leads to a dysfunctional thyroid gland and decreased secretion of thyroid hormones. If hypothyroidism is left untreated, the client may develop a **myxedema coma**, which is a life-threatening disorder that leads to hypothermia, cardiovascular collapse, hypoventilation, hyponatremia, hypoglycemia, lactic acidosis, and coma.

Symptoms of hypothyroidism include:

- Bradycardia
  - Thyroid hormones stimulate the heart, which increases the heart rate. However, in hypothyroidism, the reduced levels of thyroid hormone cause the heart rate to decrease.
- Cold intolerance
  - When thyroid hormones are low, the body's ability to generate and maintain heat is reduced. This can result in feeling excessively cold, often with a decreased tolerance to cold environments.
- Constipation
  - Thyroid hormones play a role in promoting gastric motility. With hypothyroidism, the decreased levels of thyroid hormones cause slower movement in the digestive tract, resulting in constipation.
- Fatigue and decreased energy

- Thyroid hormones are responsible for cellular metabolism and energy production. When the thyroid hormone levels are insufficient, it slows the metabolic process, resulting in decreased energy and fatigue.

- Weight gain
  - Thyroid hormones influence the body's metabolic rate and the breakdown of fat. With reduced levels of thyroid hormones, the metabolic rate slows, resulting in a decreased ability to burn calories and fat.

Treatment for hypothyroidism involves replacing the body's natural thyroid hormone when the levels are low or absent within the body and will be discussed later in this chapter.

Hyperthyroidism

Hyperthyroidism occurs when the body secretes too much T3 and T4 into the blood. The autoimmune disorder **Graves' disease** is the most common cause of hyperthyroidism. In Graves' disease, the production of TSH receptor antibodies stimulate the thyroid gland to grow and secrete additional thyroid hormone. **Thyroid storm (thyrotoxic crisis)** is a rare but severe complication of hyperthyroidism, which leads to severe tachycardia, fever, dehydration, heart failure, and coma. It occurs in clients who are inadequately treated for hyperthyroidism or initially after the removal of the thyroid.

Symptoms of hyperthyroidism include:

- Weight loss
  - Increased levels of thyroid hormones can accelerate the body's metabolic rate, causing an increase in calorie burning. This can lead to unintended weight loss, even with a normal or increased appetite.

- Heat intolerance
  - Thyroid hormones influence thermoregulation and can affect how the body generates and dissipates heat. In hyperthyroidism, the elevated levels of thyroid hormones can lead to an increased sensitivity to heat, resulting in an intolerance to hot temperatures.

- Diarrhea
  - Excessive thyroid hormones speed up gastric motility, leading to frequent bowel movements and diarrhea.

- Fine tremors
  - Increased thyroid hormones cause an increased excitability within the nervous system, leading to tremors, usually in the hands and fingers.

- Tachycardia
  - Thyroid hormones have a stimulatory effect on the heart, thereby increasing the heart rate and the force of contractions.

- Frequent mood changes
  - Thyroid hormones can influence neurotransmitters in the brain, affecting mood regulation. In hyperthyroidism, fluctuations in thyroid hormone levels contribute to mood swings, irritability, and anxiety.

- Muscle weakness
  - Elevated thyroid hormone levels can cause increased breakdown of muscle protein and impair muscle function, which leads to muscle wasting and weakness.

Treatment for hyperthyroidism includes surgery to remove all or part of the thyroid gland and antithyroid drugs, which will be discussed later in this chapter.

LINK TO LEARNING

Autoimmune Thyroid Disease

Access multimedia content (https://openstax.org/books/pharmacology/pages/27-1-introduction-to-the-thyroid-and-parathyroid)

Access Health presents an educational video on autoimmune thyroid disease.

Hypoparathyroidism

Hypoparathyroidism occurs when the body does not secrete enough PTH in the blood. This leads to dangerously low levels of calcium in the blood. Because calcium and phosphate have an inverse reaction, the phosphate levels in the body increase. Hypoparathyroidism is typically caused by an autoimmune disorder, can be idiopathic, or is a result of thyroid/parathyroid surgery.

Symptoms of hypoparathyroidism are tetany, contraction of facial muscles after tapping the facial nerve (**Chvostek sign**), induction of carpal pedal spasm (**Trousseau sign**), paresthesia, and a prolonged QT wave (total time from ventricular depolarization to complete repolarization) on an electrocardiogram. Treatment for hypoparathyroidism includes intravenous calcium gluconate, oral calcium, and vitamin D supplements, which will be discussed later in this chapter.

Hyperparathyroidism

Hyperparathyroidism occurs when the body secretes too much PTH in the blood, leading to dangerously elevated levels of calcium in the blood. The inverse reaction of calcium and phosphate causes the phosphate levels in the body to decrease. Hyperparathyroidism is typically caused by a lack of response to the normal feedback mechanism of the calcium homeostasis cycle.

Symptoms of hyperparathyroidism include:

- Nausea and vomiting
  - Elevated levels of PTH can disrupt the normal balance of calcium in the body, leading to gastrointestinal symptoms.
- Constipation
  - Excessive PTH slows gastric motility, resulting in constipation.
- Kidney stones
  - Increased levels of calcium in the blood due to hyperparathyroidism can lead to the deposition of calcium crystals in the kidneys, leading to the development of kidney stones.
- Polyuria
  - Elevated PTH levels increase the excretion of water in the urine, leading to increased urination.
- Impaired sodium-water reabsorption
  - Elevated PTH levels can interfere with the normal resorption of sodium and water in the kidneys, leading to fluid imbalance.
- Muscle weakness
  - Excessive PTH promotes the loss of calcium from muscles, impairing muscle function and causing muscle weakness.
- Bone pain and **osteoporosis**
  - Increased PTH causes increased calcium release from bones, resulting in bone pain, osteoporosis, and an increased risk of fractures.
- Depression, psychosis, or an altered mental status
  - High levels of PTH can affect neurotransmitter function, contributing to mood changes and cognitive function impairment and affecting overall mental well-being.

Treatment for hyperparathyroidism includes increasing fluid intake and supplementing with **calcimimetics**, vitamin D supplements, phosphate binders, and calcitriol, which will be discussed later in this chapter.

LINK TO LEARNING

Parathyroid Disease

Access multimedia content (https://openstax.org/books/pharmacology/pages/27-1-introduction-to-the-thyroid-and-parathyroid)
The Center for Advanced Parathyroid Surgery presents an animation video describing the parathyroid gland and causes, symptoms, and treatment for hyperparathyroidism.

Diagnostic Testing

Diagnostic testing can help determine if the thyroid and parathyroid glands are functioning appropriately. Table 27.1 provides a list of tests used to diagnose common thyroid and parathyroid conditions.

Thyroid Function Test Interpretation			
TSH (Reference range: 0.5–4.0 mU/mL)	**T4** (Reference range: 5–12 ug/dL)	**T3** (Reference range: 80–180 ng/dL)	**Condition**
Normal	Normal	Normal	None
Low	High	High	Hyperthyroidism
High	Low	Low	Hypothyroidism
Parathyroid Function Test Interpretation			
PTH (Reference range: 10–65 ng/L)	**Calcium (total serum)** (Reference range: 8.6–10.2 mg/dL)	**Phosphate** (Reference range: 3.0–4.5 mg/dL)	**Condition**
Normal	Normal	Normal	None
Low	Low	High	Hypoparathyroidism
High	High	Low	Hyperparathyroidism

TABLE 27.1 **Thyroid and Parathyroid Diagnostic Testing** (sources: American Board of Internal Medicine, 2023; Armstrong et al., 2022; Khan et al., 2022; Shahid et al., 2022; Singh & Correa, 2022)

LINK TO LEARNING

Diagnostic Testing (https://openstax.org/r/practitioner)

Diagnostic testing is key in determining thyroid and parathyroid conditions. Review the article Thyroid Function Testing in the Diagnosis and Monitoring of Thyroid Function Disorder. The first figure in the article illustrates an algorithm commonly used when diagnosing thyroid and parathyroid disorders.

Other diagnostic tests that assist in diagnosing thyroid and parathyroid conditions include:

- *Ionized serum calcium:* This test is performed for conditions that affect the body's ability to balance the amounts of ionized calcium and bound calcium in the blood. The normal range is 1.12–1.23 mmol/L, although ranges may vary slightly depending on the laboratory (American Board of Internal Medicine, 2023).
- *Vitamin D (calciferol):* This test is performed to determine the amount of vitamin D in the blood, which helps the body to absorb calcium. The normal range is 30–60 ng/mL, although ranges may vary slightly depending on the laboratory (American Board of Internal Medicine, 2023).

27.2 Thyroid and Antithyroid Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 27.2.1 Identify the characteristics of thyroid and antithyroid drugs used to treat thyroid disorders.
- 27.2.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of thyroid and antithyroid drugs used to treat thyroid disorders.
- 27.2.3 Describe nursing implications of thyroid and antithyroid drugs used to treat thyroid disorders.
- 27.2.4 Explain the client education related to thyroid and antithyroid drugs used to treat thyroid disorders.

Thyroid Drugs

Thyroid drugs are used when the thyroid is functioning incorrectly and there is a need to replace the thyroid hormone so that the body can maintain its expected function. Thyroid drugs can be synthetic thyroid hormones or animal-based thyroid hormones. These drugs act by replacing the body's natural thyroid hormone when the levels are low or absent within the body.

Levothyroxine Sodium

Levothyroxine sodium is a synthetic thyroid hormone that is identical to T4 produced in the body. The gastrointestinal tract absorbs 40%–80% of this synthetic hormone. The drug is greater than 99% protein bound and easily distributed. It is primarily eliminated by the kidneys, with approximately 20% of T4 being excreted in the stool (Eghtedari & Correa, 2022). It comes in tablet and injectable forms and is used to treat hypothyroidism and pituitary TSH suppression. Levothyroxine is contraindicated in clients with uncorrected adrenal insufficiency: because of the role of adrenal glands in regulating stress response and cortisol production, levothyroxine's ability to increase metabolic demands and stress may overwhelm the impaired adrenal glands, causing an adrenal crisis. Stabilization of adrenal function is crucial before starting levothyroxine treatment to prevent an adrenal crisis.

Levothyroxine sodium has a narrow therapeutic index; careful dose titration is necessary to avoid overtreatment or undertreatment. Clients should take this drug in the morning at least 30 minutes before consuming food or fluid containing caffeine such as coffee, tea, or soda. Food and caffeinated drinks can both interfere with the absorption of levothyroxine sodium.

Liothyronine Sodium

Liothyronine sodium is a synthetic thyroid hormone mimicking T3. This hormone replacement is commonly used to treat hypothyroidism and myxedema coma. Liothyronine can be taken orally, comes in an intravenous form, and is easily absorbed and readily distributed in the body. As with levothyroxine, liothyronine is contraindicated in clients with uncorrected adrenal insufficiency. As stated above, the adrenal glands control the stress response and cortisol levels within the body. When they are impaired, they are unable to handle the increase in metabolic rate caused by the administration of liothyronine, leading to an adrenal crisis. Adverse effects of liothyronine include anxiety, blurred vision, chest discomfort, decreased bone mineral density, and decreased urine output.

SAFETY ALERT

Similarly Named Drugs

Do not confuse *levothyroxine* sodium with *liothyronine* sodium. Although these drugs are in the same drug class, they require different dosing and lab monitoring.

Desiccated Thyroid Extract

Desiccated thyroid extract is a thyroid hormone developed from pig glands that is often used as an over-the-counter remedy for thyroid hormone replacement. Desiccated thyroid extract has not been approved by the Food and Drug Administration (FDA) due to a complex manufacturing process leading to issues with safety, effectiveness, and quality, with inconsistent or inaccurate dosage. Table 27.2 lists common thyroid drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Levothyroxine sodium (Synthroid, Levoxyl)	Individualized dosing due to a narrow therapeutic index. Standard dosing starts at 1.6 mcg/kg/day orally; increase by 12.5–25 mcg orally every 4–6 weeks if needed. Serum T4 levels should be used to monitor therapeutic dosing range of drug. Must be titrated based on the individual's need and to avoid the consequences of overtreatment or undertreatment.
Liothyronine sodium (Cytomel, Triostat)	25 mcg orally once daily; increase by 25 mcg orally daily every 1–2 weeks if needed. Maintenance dose: 25–75 mcg once daily. Serum T3 levels should be used to monitor therapeutic dosing range of drug.

TABLE 27.2 **Drug Emphasis Table: Thyroid Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects among the thyroid drug classification include cardiac effects—such as tachycardia, palpitations, and arrhythmias—weight loss, nervousness and irritability, heat intolerance, diarrhea, abdominal cramping, headaches, and sleep disturbances.

Contraindications for thyroid drug classification include hypersensitivity to the drug or any of its components as well as any recent myocardial infarction because thyroid drugs can increase heart rate and heart contractility. Untreated adrenal insufficiency is a contraindication because impaired adrenal glands cannot handle the increased metabolic rate cause by thyroid drugs, as is hyperthyroidism since the drugs would increase thyroid hormone levels that are already elevated.

Table 27.3 is a drug prototype table for thyroid drugs featuring levothyroxine sodium. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Thyroid hormone **Mechanism of Action** Replaces the amount of hormone the thyroid is unable to produce, helping to restore thyroid hormone homeostasis within the body	**Drug Dosage** Individualized dosing due to a narrow therapeutic index. Standard dosing starts at 1.6 mcg/kg/day orally; increase by 12.5–25 mcg orally every 4–6 weeks if needed. Serum T4 levels should be used to monitor therapeutic dosing range of drug. Must be titrated based on the individual's need and to avoid the consequences of overtreatment or undertreatment.
Indications Hypothyroidism Pituitary TSH suppression **Therapeutic Effects** Restores thyroid hormone levels to normal Maintains thyroid hormone homeostasis	**Drug Interactions** Dopamine Glucocorticoids Octreotide Amiodarone Digitalis Iodine Lithium Calcium Iron Warfarin **Food Interactions** Soy Soybean flour Cotton seed meal Walnuts Dietary fiber may bind to levothyroxine sodium and decrease its absorption
Adverse Effects Irregular heartbeat Heat intolerance Irregular breathing Irritability Nausea Tremors Decreased urine output	**Contraindications** Adrenal insufficiency Nontoxic goiter or nodular thyroid disease Caution: Monitor closely when administering to older clients who have underlying cardiovascular disease—may precipitate thyrotoxicosis

TABLE 27.3 **Drug Prototype Table: Levothyroxine Sodium** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking thyroid drugs:

- Educate the client that thyroid replacement hormone is a lifelong therapy.
- Assess the client's knowledge about signs and symptoms of over- and undertreatment, adverse reactions, and contraindications and clarify any gaps in knowledge.
- Monitor thyroid functioning of the client and report any abnormalities or symptoms of thyroid storm, such as tachycardia, cardiac dysrhythmias, fever, heart failure, flushed skin, confusion, behavioral changes, and hypotension, to the health care provider.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a thyroid drug should:

- Take on an empty stomach 1/2–1 hour before breakfast for better absorption.
- Keep a journal of their symptoms. It may take several weeks for them to notice improved symptoms.
- Report symptoms of irregular heartbeat, chest pain, shortness of breath, leg cramps, headache, nervousness, irritability, sleeplessness, and heat intolerance to their health care provider because these may represent an adverse reaction or toxicity to the drug.
- Notify the health care provider if they are pregnant or become pregnant because the dose of the drug may need to be increased during pregnancy.
- Store out of reach of children and away from heat, moisture, and light.

The client taking a thyroid drug *should not*:

- Stop taking unless directed by their health care provider because this drug class replaces their body's missing thyroid hormone.
- Take with food because it will decrease the drug's absorption.
- Take within 4 hours of taking calcium and/or iron supplements, including calcium antacids, because they may impact the drug's absorption.

FDA BLACK BOX WARNING

Thyroid Hormones

Thyroid hormones, including levothyroxine sodium, either alone or with other therapeutic agents, should not be used for treatment of obesity or weight loss due to producing serious toxicity or life-threatening manifestations.

Antithyroid Drugs

Antithyroid drugs are used to inhibit production of the thyroid hormone so that the body can maintain normal thyroid homeostasis. Antithyroid drugs act by inhibiting the synthesis of thyroid hormones or by inundating the thyroid gland with iodine to prevent thyroid hormone release. Antithyroid drugs are used when the thyroid hormone levels are elevated within the body.

Thionamides

Thionamides are compounds that effectively hinder the synthesis of thyroid hormones. These compounds are transported into the thyroid gland and act by inhibiting two critical processes: **organification** of iodine to tyrosine residues in **thyroglobulin** as well as coupling of **iodotyrosines**, leading to lower serum levels of thyroid hormones. The process of organification of iodine to tyrosine residues refers to the incorporation of iodine atoms into tyrosine amino acid molecules within the structure of thyroglobulin, a protein produced by the thyroid gland. This is an essential step in the synthesis of thyroid hormones. The coupling of iodotyrosines refers to the binding together of iodinated tyrosine molecules within the thyroglobulin to form the final thyroid hormones T3 and T4. Thionamides are used in the treatment of hyperthyroidism and Graves' disease. Thionamides include methimazole and propylthiouracil.

Methimazole

Methimazole inhibits the synthesis of thyroid hormones and is indicated to treat hyperthyroidism. This medication is rapidly absorbed in the gastrointestinal tract and metabolized rapidly. It is excreted mainly in the urine but is excreted in breast milk and should be used cautiously with clients who are breastfeeding. Careful dose titration is necessary to avoid overtreatment or undertreatment. When the client develops toxicity to methimazole, symptoms such as nausea, vomiting, epigastric distress, headache, fever, joint pain, pruritus, edema, and agranulocytosis may develop (Armstrong et al., 2022; DailyMed, *Methimazole,* 2022; Shahid et al., 2022; Singh & Correa, 2022).

Propylthiouracil

Propylthiouracil inhibits the synthesis of thyroid hormones. This drug is readily absorbed and extensively metabolized; it is mainly excreted in the urine. Propylthiouracil is indicated for Graves' disease with hyperthyroidism, multinodular **goiter**, and to ameliorate symptoms of hyperthyroidism before thyroidectomy or radioactive iodine therapy in clients who did not tolerate methimazole. It is contraindicated in clients with hypersensitivity and with liver failure. Adverse effects include hepatitis, jaundice, anemia, thrombocytopenia, nephritis, arthralgia, and paresthesia.

Iodine

The body naturally uses **iodine** for the formation of thyroid hormone. Iodine solutions cause the thyroid cells to become inundated with iodine, thereby decreasing thyroid hormone production. Iodine preparations are used to treat hyperthyroidism when thionamides are ineffective or for those clients who are not candidates for surgery.

Potassium Iodide

Potassium iodide prevents iodine from getting into the thyroid gland. As a medication, potassium iodine is used two separate ways: 1) to treat hyperthyroidism by inhibiting thyroid hormone secretion in very acute situations, and 2) to prevent the uptake of radioactive iodine in the event of a nuclear emergency. Additional use includes radioactive iodine to ablate a hyperactive thyroid gland. Adverse effects include skin rash, shortness of breath, wheezing, swelling, fever, and joint pain. It is contraindicated in those who have had an allergic reaction to iodine and those with nodular thyroid disease. ThyroShield and Thyrosafe are the only FDA-approved brands of potassium iodide.

Table 27.4 lists common antithyroid drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Methimazole (Tapazole)	*Mild hyperthyroidism:* 15 mg orally daily. *Moderate hyperthyroidism:* 30–40 mg orally daily. *Severe hyperthyroidism:* 60 mg orally daily, divided into 3 doses at 8-hour intervals. *Maintenance dose:* 5–15 mg orally daily.
Propylthiouracil (PTU)	300–400 mg orally daily; maintenance dose 100–150 mg orally daily.
Potassium iodide (Thyrosafe)	130 mg orally daily at 24-hour intervals.

TABLE 27.4 **Drug Emphasis Table: Antithyroid Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects include:

- Rash or skin reactions—pruritis and hives
- Gastrointestinal symptoms—nausea and vomiting
- Liver toxicity—jaundice, dark urine, abdominal pain, fatigue
- Bone marrow suppression—decreased white blood cell, red blood cell, and platelet production leading to unexplained fever, sore throat, easy bruising, bleeding, and fatigue
- Hypothyroidism—increased fatigue, weight gain, cold intolerance, constipation

Contraindications include hypersensitivity to the drug or any of its components, severe liver disease or impairment, and with pregnancy or breastfeeding because the drugs can cross the placenta, be excreted in breast milk, and potentially affect the development of the fetus or infant.

Table 27.5 is a drug prototype table for antithyroid drugs featuring methimazole. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antithyroid agent **Mechanism of Action** Inhibits the synthesis of thyroid hormones and thus is effective in the treatment of hyperthyroidism	**Drug Dosage** *Mild hyperthyroidism:* 15 mg orally daily. *Moderate hyperthyroidism:* 30–40 mg orally daily. *Severe hyperthyroidism:* 60 mg orally daily, divided into 3 doses at 8-hour intervals. *Maintenance dose:* 5–15 mg orally daily.
Indications Hyperthyroidism Ameliorating hyperthyroidism in preparation for subtotal thyroidectomy or radioactive iodine therapy When thyroidectomy is contraindicated or not advisable **Therapeutic Effects** Lowers thyroid hormone levels Relieves/reduces manifestations of hyperthyroidism	**Drug Interactions** Anticoagulants Beta-adrenergic blockers Digitalis glycosides Theophylline **Food Interactions** No significant interactions
Adverse Effects Agranulocytosis Thrombocytopenia Aplastic anemia Fever Insulin autoimmune syndrome (low blood glucose levels) Jaundice Urticaria Epigastric distress Arthralgia	**Contraindications** Hypersensitivity Pregnancy and breastfeeding Caution: Monitor closely for agranulocytosis and hepatotoxicity

TABLE 27.5 **Drug Prototype Table: Methimazole** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antithyroid drugs:

- Monitor complete blood cell count and coagulation studies, liver studies, and thyroid levels and report abnormalities to the health care provider.
- Check with the health care provider before administering antithyroid drugs if the client is currently taking anticoagulants, beta-adrenergic blockers and digitalis glycosides, or theophylline, which stimulates the central nervous system and when taken with antithyroid drugs can impact mood, behavior, cognition, and sleep patterns.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antithyroid drug should:

- Take the drug exactly as prescribed by the health care provider.
- Report sore throat, skin eruptions, fever, headache, or general malaise to the health care provider because these may be symptoms of a severe reaction.
- Monitor weight weekly and report a weight gain of 3 pounds in 24 hours or 5 pounds in a week to the health care provider.
- Notify the health care provider if they are pregnant or plan to become pregnant or if they are breastfeeding.
- Store out of reach of children and away from heat, moisture, and light.

The client taking an antithyroid drug *should not:*

- Eat dietary sources of iodine (iodized salt, shellfish) without speaking with the health care provider first.

FDA BLACK BOX WARNING

Propylthiouracil

Severe liver injury and acute liver failure have been reported in clients treated with propylthiouracil.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Ellis Dominico is a 40-year-old client who visits their primary health care provider's office for a checkup. Ellis reports fatigue and decreased energy, constipation, and having an intolerance to cold temperatures.

History
Hyperthyroidism (diagnosed 6 months ago)

Current Medications
Methimazole, 15 mg orally daily

Vital Signs		Physical Examination
Temperature:	98.3°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; no peripheral edema noted; S1, S2 auscultated, rhythm regular • *Respiratory:* Lungs clear to auscultation bilaterally • *GI:* Abdomen firm, nontender, slightly distended • *GU:* Client reports urinary output unchanged from their baseline • *Neurological:* Lethargy and slow speech noted; no other neurological deficits noted • *Integumentary:* No wounds noted; skin appropriate for age
Blood pressure:	96/58 mm Hg	
Heart rate:	58 beats/min	
Respiratory rate:	18 breaths/min	
Oxygen saturation:	95% on room air	
Height:	5'6"	
Weight:	211 lb (10 lb heavier than weight 3 months ago)	

TABLE 27.6

1. Based on the assessment findings, which health condition does the nurse anticipate the health care provider will identify?
   a. Hyperthyroidism
   b. Hypothyroidism
   c. Hyperparathyroidism
   d. Hypoparathyroidism

2. Which diagnostic test should the nurse anticipate the health care provider will order for Ellis?
   a. Serum ionized calcium
   b. Serum total calcium
   c. PTH
   d. TSH

27.3 Calcium Preparations, Vitamin D, Bisphosphonates, Calcimimetics, and Peptide Hormones

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 27.3.1 Identify the characteristics of calcium preparations, vitamin D, bisphosphonates, calcimimetics, and peptide hormone drugs used to treat hypoparathyroidism.
- 27.3.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of calcium preparations, vitamin D, bisphosphonates, calcimimetics, and peptide hormone drugs used to treat hypoparathyroidism.
- 27.3.3 Describe nursing implications of calcium preparations, vitamin D, bisphosphonates, calcimimetics, and peptide hormone drugs used to treat hypoparathyroidism.
- 27.3.4 Explain the client education related to calcium preparations, vitamin D, bisphosphonates, calcimimetics, and peptide hormone drugs used to treat hypoparathyroidism.

This section of the chapter discusses drugs used to treat parathyroid dysfunction. These drugs are used when parathyroid functioning is decreased or when calcium needs to be replaced or decreased to maintain its expected functions within the body.

Calcium Preparations

Calcium is a mineral utilized by the body to promote bone health. It also plays a role in blood clotting, muscle contraction, regulating heart rhythm, nerve function, and cell communication. Vitamin D is needed for the body to be able to absorb calcium. The two are often prescribed together.

The recommended daily amount of calcium is 1000–2000 mg for adults. Calcium can be found in many foods including dairy products such as milk, yogurt, and cheese; fish such as sardines and salmon; vegetables such as kale, broccoli, and cabbage; soy milk; almond milk; and tofu.

SPECIAL CONSIDERATIONS

Calcium and Race/Ethnicity, Age, and Socioeconomic Factors

In the United States, many Black and Asian people, as well as many adults experiencing poverty, aged 50 years and older, are less likely to get the recommended daily amounts of calcium (National Institutes of Health, 2023). As we age, our bodies absorb less calcium. For postmenopausal clients, a decrease in calcium absorption can lead to conditions such as osteoporosis.

Access multimedia content (https://openstax.org/books/pharmacology/pages/27-3-calcium-preparations-vitamin-d-bisphosphonates-calcimimetics-and-peptide-hormones)
This video on the role and importance of vitamin D (calcitriol) explains why vitamin D is vital for proper absorption and utilization of calcium.

Calcium

Some calcium supplements are available over the counter and are not regulated by the FDA. Clients should speak with their health care provider before starting any over-the-counter medication.

Calcium Acetate

Calcium acetate is used in the treatment of hypocalcemia and hyperphosphatemia but is contraindicated in clients with hypercalcemia. This phosphate binder, which comes in capsule form, reduces serum phosphate levels, thereby increasing serum calcium levels. Adverse effects include nausea, vomiting, constipation, gas, bloating, and headache.

Calcium Carbonate

Calcium carbonate is used in the treatment of hypocalcemia and can also be used as an antacid; it is contraindicated in clients with hypercalcemia. Like calcium acetate, this supplement reduces serum phosphate levels and results in increased serum calcium levels. This medication is available in a tablet, chewable tablet, capsule, and liquid.

Adverse effects include upset stomach, vomiting, abdominal pain, bloating, constipation, dry mouth, loss of appetite, metallic taste, and increased urination.

Calcium Chloride

Calcium chloride is an injectable drug used in the treatment of hypocalcemia in those clients requiring a prompt increase in plasma calcium levels. Calcium chloride is contraindicated in cardiac resuscitation and for use in clients with hypercalcemia. It is administered via the intravenous route only. Adverse effects include vasodilation, decreased blood pressure, tingling sensation, and calcium taste (bitter and sour). Administration site reactions include local soft tissue inflammation, local necrosis, and extravasation.

Calcium Gluconate

Calcium gluconate is an injectable drug used in the treatment of acute symptomatic hypocalcemia. It increases serum ionized calcium levels. This medication is contraindicated in clients with hypercalcemia and in neonates (28 days old or younger) and should be used cautiously in clients with cardiac arrhythmias with concomitant cardiac glycoside use. Adverse effects include vasodilation, decreased blood pressure, cardiac arrhythmia, syncope, and cardiac arrest. Administration site reactions include local soft tissue inflammation, local necrosis, and extravasation.

Table 27.7 lists common calcium drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Calcium acetate (PhosLo, Eliphos)	*Hyperphosphatemia (in chronic kidney disease):* 1334 mg orally daily with each meal.
Calcium carbonate (Maalox, Tums)	*Mild hypocalcemia:* 500 mg orally daily. *Adults and children over 12 years of age:* Chew 2–4 tablets as symptoms occur. *Maximum dose:* Do not take more than 8 tablets in 24 hours. Do not use the maximum dose for more than 2 weeks.
Calcium chloride ($CaCl$, $CaCl_2$)	Individualized dosing by health care provider based on laboratory values. Usual adult dosage in hypocalcemic disorders: 200–1000 mg; slow intravenous push at intervals of 1–3 days depending on response of the client and/or serum ionized calcium determinations.
Calcium gluconate (Kalcinate)	*Acute symptomatic hypocalcemia:* Individualized dosing by health care provider based on laboratory values. Standard dosing starts at 1000–2000 mg intravenously initially; subsequent doses of 1000–2000 mg intravenously every 6 hours based on laboratory values (available in 100 mg/mL).

TABLE 27.7 **Drug Emphasis Table: Calcium Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects include kidney stones and gastrointestinal symptoms, such as constipation, bloating, abdominal discomfort, and flatulence. Drugs, such as tetracycline antibiotics, bisphosphates (e.g., alendronate), and thyroid hormone replacements, can interfere with calcium absorption so should be taken at separate times to minimize interactions. Hypercalcemia, another common adverse effect, leads to symptoms such as fatigue, confusion, constipation, increased thirst, and frequent urination.

Contraindications include hypersensitivity to the drug or any of its components. This medication is contraindicated for hypercalcemia because it will increase calcium levels in the blood and for hyperparathyroidism because increased calcium can worsen this condition. Kidney stones, as calcium preparation, may contribute to the formation of new kidney stones. Malabsorption syndrome, such as Celiac disease or Crohn's disease, may occur because calcium may not be absorbed appropriately by the body with these conditions.

Table 27.8 is a drug prototype table for calcium carbonate. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Calcium preparation, antacid, and phosphate binder **Mechanism of Action** Acts in the small intestine by chelating with oxalate to prevent phosphate absorption, is absorbed in the small intestines to help circulate ionized calcium in the blood, inhibits pepsin and bile acid, increases gastric motility, and initiates peristalsis	**Drug Dosage** *Mild hypocalcemia:* 500 mg orally daily. *Adults and children over 12 years of age:* Chew 2–4 tablets as symptoms occur. *Maximum dose:* Do not take more than 8 tablets in 24 hours. Do not use the maximum dose for more than 2 weeks.
Indications Hypocalcemia Hypothyroidism Hypoparathyroidism Osteoporosis Osteomalacia As a calcium supplement in postmenopausal clients and during pregnancy **Therapeutic Effects** Improves calcium levels within the body Reduces heartburn and gastroesophageal reflux disease Increases gut motility	**Drug Interactions** Digoxin Phosphate supplements Sodium polystyrene sulfonate **Food Interactions** No significant interactions
Adverse Effects GI symptoms (upset stomach, vomiting, abdominal pain, bloating, constipation) Dry mouth Loss of appetite Metallic taste Increased urination	**Contraindications** Hypersensitivity Hypercalcemia Caution: Monitor closely for kidney stones

TABLE 27.8 **Drug Prototype Table: Calcium Carbonate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Vitamin D

Vitamin D is a fat-soluble vitamin that promotes calcium and phosphorous absorption in the intestines and helps to maintain adequate serum calcium and phosphate levels within the body. Vitamin D has other roles in the body—it reduces inflammation, and it stimulates insulin production in the modulation of cell function, neuromuscular and immune system function, and in glucose metabolism (Chauhan et al., 2022).

Vitamin D has two forms, vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). Both forms are well absorbed by the gastrointestinal tract. The recommended daily allowance (RDA) of vitamin D for adults is 600–800 IU; however, replacement regimens for those with low vitamin D levels vary from the RDA.

Few foods naturally contain vitamin D. Those that do include trout, salmon, tuna, fish liver oils, beef liver, some mushrooms, and egg yolks. Some dairy products such as milk and cheeses are fortified with vitamin D. Sunlight is required for vitamin D synthesis; however, the FDA recommends sun protection such as sunscreen and limiting exposure to high sun times of day to prevent sun exposure complications such as skin cancer.

Ergocalciferol

Ergocalciferol is a synthetic calcium regulator. It mobilizes calcium and phosphate from bone and increases reabsorption of calcium and phosphate by the renal tubules, thereby increasing serum calcium and phosphate levels. This supplement is indicated in the treatment of hypoparathyroidism and in those with hypophosphatemia. It is frequently used off-label for vitamin D deficiency. It is contraindicated in clients with hypercalcemia, malabsorption syndrome, and hypervitaminosis D as well as clients with abnormal sensitivity to the toxic effects of vitamin D.

Calcitriol

Calcitriol is a synthetic vitamin D analog that is active in the regulation and absorption of calcium from the gastrointestinal tract. Calcitriol is readily absorbed from the intestine with peak serum concentration within 3–6 hours. It is 99.9% bound to protein in the blood and easily distributed. Calcitriol is indicated in the management of hypocalcemia and hypoparathyroidism. It is contraindicated in clients with hypercalcemia or evidence of vitamin D toxicity.

Table 27.9 lists common vitamin D drugs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Ergocalciferol (Drisdol)	*Hypoparathyroidism:* *Adults:* 50,000–200,000 units daily concomitantly with calcium lactate 4 g, 6 times daily.
Calcitriol (Rocaltrol)	*Hypoparathyroidism:* *Adults:* 0.25 mcg orally daily in the morning; dose may be increased by health care provider in 2–4 weeks based on lab values. *Children (≥3 years of age):* 0.25 mcg orally daily; maximum dose 0.50 mcg orally daily.

TABLE 27.9 Drug Emphasis Table: Vitamin D (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects include constipation, dry mouth, bone pain, metallic taste, polyuria, pruritis, increased liver enzymes (AST), and elevated blood urea nitrogen (BUN) levels.

Contraindications include hypersensitivity to the drug or any of its components, malabsorption disorders (such as Celiac disease or Crohn's disease), vitamin D toxicity (symptoms include recurrent vomiting, confusion, apathy, and dehydration), and hypercalcemia (symptoms include nausea and vomiting, abdominal pain, and weight loss).

Table 27.10 is a drug prototype table for the vitamin D drug calcitriol. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Vitamin D analog **Mechanism of Action** Acts on cells in the gastrointestinal tract to increase the production of calcium transport proteins (calbindin-D proteins), which results in increased uptake of calcium from the intestines into the body	**Drug Dosage** *Hypoparathyroidism:* *Adults:* 0.25 mcg orally daily in the morning; dose may be increased by health care provider in 2–4 weeks based on lab values. *Children (≥3 years of age):* 0.25 mcg orally daily; maximum dose 0.50 mcg orally daily.
Indications Hypocalcemia Hypoparathyroidism Hemodialysis clients with hyperphosphatemia **Therapeutic Effects** Increases serum calcium levels	**Drug Interactions** Cholestyramine Phenytoin Thiazides Ketoconazole Mineral oil **Food Interactions** No significant interactions
Adverse Effects *Early reactions:* Weakness Headache Somnolence Nausea/vomiting Dry mouth Constipation Bone pain Metallic taste *Late reactions:* Polyuria Polydipsia Anorexia/weight loss Nocturia Pancreatitis Photophobia Pruritus Hyperthermia Elevated BUN Elevated liver enzymes Hypertension Cardiac arrhythmias	**Contraindications** Hypersensitivity Hypercalcemia Vitamin D toxicity Caution: Use cautiously in clients with renal and hepatic impairment

TABLE 27.10 **Drug Prototype Table: Calcitriol** (source: https://dailymed.nlm.nih.gov/dailymed/)

Bisphosphonates

Bisphosphonates are pyrophosphate analogues. They are divided into two groups: nitrogen-containing bisphosphonates and non-nitrogen-containing bisphosphonates that are not approved by the FDA in the treatment of osteoporosis. The nitrogen-containing agents are used in the treatment of osteoporosis and other associated conditions where bones are thin, fragile, and at an increased risk for fracture. Bisphosphonates inhibit bone resorption by attaching to hydroxyapatite binding sites on the bone. As **osteoclasts** resorb bone, the bisphosphonate embedded in the bone is released and impairs the osteoclast's ability to continue bone resorption, thereby improving bone density (Ganesan at el., 2022).

Alendronate

Alendronate is a nitrogen-containing bisphosphonate that inhibits bone resorption and improves bone density. It is used in prevention and treatment of osteoporosis and to increase bone mass in male and female clients. This medication should be taken with 6–8 ounces of water, and the client should sit/stand for at least 30 minutes after administration to prevent esophageal irritation. Alendronate is contraindicated with esophageal abnormalities, the inability to stand/sit upright for 30 minutes, hypocalcemia, and hypersensitivity. Adverse effects include abdominal pain, acid regurgitation, constipation, diarrhea, dyspepsia, musculoskeletal pain, and nausea.

Ibandronate

Ibandronate is a potent nitrogen-containing bisphosphonate that is indicated for the treatment and prevention of postmenopausal osteoporosis and is available in tablet and injectable formulation. Oral dosing of ibandronate should be on an empty stomach with 6–8 ounces of water. The client should sit or stand for at least 60 minutes after administration to enhance absorption and prevent esophageal inflammation. This medication is contraindicated in clients with hypocalcemia, hypersensitivity, pregnancy, and abnormalities of the esophagus that delay emptying and those with the inability to sit/stand for at least 60 minutes after taking this drug. Adverse effects include back pain, dyspepsia, pain in extremities, diarrhea, headache, and myalgia.

Risedronate

Risedronate is also a nitrogen-containing bisphosphonate that is indicated in the treatment of postmenopausal osteoporosis. It is available as a delayed-release and immediate-release tablet and should be taken in the morning immediately following breakfast. The client should be able to sit/stand for at least 30 minutes following administration to facilitate delivery to the stomach and to avoid esophageal irritation. The delayed-release tablet should not be chewed, crushed, or cut. Risedronate is contraindicated in clients with hypocalcemia, with abnormalities of the esophagus that delay emptying, who are unable to sit/stand for at least 30 minutes after taking this drug, with hypersensitivity, and who are pregnant. Adverse effects include abdominal pain, constipation/diarrhea, nausea/vomiting, bronchitis, arthralgia, back pain, musculoskeletal pain, pain in the extremities, myalgia, dizziness, and headache.

Table 27.11 lists common bisphosphonate drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Alendronate (Fosamax)	*Treatment of osteoporosis:* *Daily dosing:* 5–10 mg orally in the morning. *Weekly dosing:* 70 mg orally in the morning.
Ibandronate (Boniva)	*Treatment of osteoporosis:* 150 mg orally once monthly *or* 3 mg intravenously 3 times a month.
Risedronate sodium (Actonel)	*Treatment of osteoporosis:* *Immediate-release tablet:* 5 mg orally once daily *or* 35 mg orally once weekly *or* 150 mg orally once monthly. *Delayed-release tablet:* 35 mg orally once weekly in the morning.

TABLE 27.11 Drug Emphasis Table: Bisphosphonates (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of bisphosphonates drug class include gastrointestinal symptoms (such as abdominal pain, dyspepsia, nausea, vomiting, and diarrhea), esophageal irritation (leading to heartburn and difficulty swallowing), musculoskeletal pain, **osteonecrosis** of the jaw (death of bone tissue in the jaw leading to pain, swelling, infection, and exposed bone in severe cases), and atypical fractures.

Contraindications include hypersensitivity to the drugs or any of their components as well as severe renal impairment because these drugs are primarily excreted through the kidneys and use of these drugs can further impair kidney function. This class of drugs is also contraindicated in clients who have an inability to sit upright or stand for at least 30–60 minutes after taking the medication.

Table 27.12 is a drug prototype table for the bisphosphonate drug alendronate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Bisphosphonate—nitrogen-containing **Mechanism of Action** Inhibits bone resorption to mineral surfaces and subsequent internalization by bone-resorbing osteoclasts where they interfere with biochemical processes and therefore improve bone density	**Drug Dosage** *Treatment of osteoporosis:* *Daily dosing:* 5–10 mg orally in the morning. *Weekly dosing:* 70 mg orally in the morning.
Indications Osteoporosis in postmenopausal clients Paget's disease Glucocorticoid-induced osteoporosis **Therapeutic Effects** Increases bone mass	**Drug Interactions** Calcium supplements Antacids Aspirin Nonsteroidal anti-inflammatories (NSAIDs) **Food Interactions** No significant interactions
Adverse Effects Abdominal pain Acid regurgitation Constipation/diarrhea Dyspepsia Nausea Musculoskeletal pain	**Contraindications** Hypersensitivity Hypocalcemia Abnormalities of the esophagus that delay emptying Inability to sit/stand upright for at least 30 minutes Pregnancy

TABLE 27.12 **Drug Prototype Table: Alendronate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Calcimimetics

Calcimimetics are drugs that mimic the actions of calcium by allosteric activation of the calcium-sensing receptor (CaSR) in the parathyroid glands or other tissues. These drugs lower the activation of extracellular calcium ions and decrease PTH release, thus reducing the amount of calcium in the blood. Calcimimetics are used in the treatment of hyperparathyroidism and in clients who have hypercalcemia.

Cinacalcet

Cinacalcet is a positive modulator of the CaSR agonist and is indicated in the treatment of primary and secondary hyperparathyroidism and in the treatment of hypercalcemia. This medication should be taken with meals, and the tablet should not be chewed, crushed, or divided. Nurses should use cinacalcet cautiously in clients with upper gastrointestinal bleeding, those with hypotension and/or heart failure, and those with bone disease. Adverse effects include nausea and vomiting.

Adverse Effects and Contraindications

Adverse effects of calcimimetics include gastrointestinal symptoms such as nausea, vomiting, and abdominal pain; hypocalcemia where symptoms include muscle cramps, tingling, numbness in the fingers or lips, and seizures; hypophosphatemia where symptoms include muscle weakness, bone pain, and impaired energy metabolism; and adynamic bone disease, which is characterized by low bone turnover and increased risk of fractures.

Contraindications include hypersensitivity to the drug or any of its components and in those clients with hypocalcemia because this can cause further decrease in calcium levels and death. Calcimimetics should be used cautiously in clients with severe liver impairment because they are primarily metabolized by the liver and can further impair its function.

Table 27.13 is a drug prototype table for the calcimimetics drug cinacalcet. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Calcimimetic **Mechanism of Action** Amplifies the calcium-sensing receptor (CaSR) in the parathyroid gland, thereby suppressing PTH levels and in turn reducing blood calcium levels	**Drug Dosage** *Secondary hyperparathyroidism in clients with chronic kidney disease on dialysis:* Recommended starting dose is 30 mg orally once daily. Serum calcium and serum phosphate levels should be measured within 1 week, and intact PTH (iPTH) should be measured 1–4 weeks after initiation. Dose adjustment should be titrated every 2–4 weeks through sequential dosing of 30, 60, 90, 120, and 180 mg orally once daily to target iPTH levels of 150–300 pg/mL.
Indications Primary and secondary hyperparathyroidism For the treatment of hypercalcemia in adults with parathyroid carcinoma **Therapeutic Effects** Reduces calcium levels in the blood	**Drug Interactions** CYP3A4 (such as ketoconazole, itraconazole) CYP2D6 (such as desipramine, metoprolol, and carvedilol) **Food Interactions** No significant interactions
Adverse Effects Nausea/vomiting Abdominal pain Muscle cramps Bone pain Increased risk for fractures	**Contraindications** Hypersensitivity Hypocalcemia Caution: Use cautiously in clients with severe liver impairment as cinacalcet is primary metabolized by the liver and can further impair its function

TABLE 27.13 **Drug Prototype Table: Cinacalcet** (source: https://dailymed.nlm.nih.gov/dailymed/)

Peptide Hormones

Peptide hormones are synthetic analog hormones used in the treatment of various disease processes. For this chapter, calcitonin salmon will be covered under this drug classification. This type of peptide hormone inhibits osteoclasts and increases renal excretion of calcium, thereby decreasing serum calcium levels. In the renal tubules, it reduces serum calcium and phosphate by promoting diuresis and decreasing reabsorption. In bone, this peptide hormone causes osteoclasts to contract, which reduces their motility and ability to resorb bone. For these reasons, this medication is used to treat postmenopausal osteoporosis, **Paget's disease** of bone, and emergent hypercalcemia (Wang et al., 2022).

Calcitonin Salmon

Calcitonin salmon is a synthetic peptide hormone that is used in the treatment of hypercalcemia, postmenopausal osteoporosis when alternative therapies are not suitable, and symptomatic Paget's disease. Calcitonin salmon is available as an injectable and nasal spray and is contraindicated in clients with hypersensitivity. Adverse effects of nasal administration include nasal reactions such as dryness and irritation, nausea with or without vomiting, injection site inflammation, and flushing of face or hands.

For preparation and administration of injectable calcitonin salmon, the client should visually inspect the injection vials to ensure the solution is clear and colorless. If the solution is not clear and colorless or contains any particles or if the vial is damaged, the client should discard the solution. If the volume of the drug exceeds 2 mL, intramuscular injection is preferable. The client should be instructed on how to use the sterile injection technique and to dispose of needles properly (DailyMed, *Calcitonin Salmon Injection,* 2023).

Adverse Effects and Contraindications

Adverse effects of peptide hormones include nasal dryness and irritation, nausea with or without vomiting, injection site inflammation, and flushing of hands or face.

Contraindications for peptide hormones include hypersensitivity to the drug or any of its components.

Table 27.14 is a drug prototype table for the peptide hormone drug calcitonin salmon. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Peptide hormone **Mechanism of Action** Inhibits osteoclasts, the cells that breakdown existing bone, thereby decreasing the rate of bone breakdown	**Drug Dosage** *Hypercalcemia:* Recommended starting dose: 4 USP units/kg body weight every 12 hours by subcutaneous or intramuscular injection. If response is not satisfactory after 1–2 days, the dose may be increased to 8 USP units/kg every 12 hours. If the response remains unsatisfactory after 2 more days, the dose may be further increased to a maximum of 8 USP units/kg every 6 hours. *Postmenopausal osteoporosis:* In clients more than 5 years postmenopause: 100 USP units (0.5 mL) daily administered subcutaneously or intramuscularly. Nasal spray is one spray (200 USP calcitonin salmon units) daily administered intranasally, alternating nostrils daily. *Paget's disease:* 100 USP units (0.5 mL) daily administered subcutaneously or intramuscularly.
Indications Hypercalcemia Postmenopausal osteoporosis Paget's disease of the bone **Therapeutic Effects** Decreases the rate of bone breakdown	**Drug Interactions** No signification interactions **Food Interactions** No significant interactions
Adverse Effects Nasal dryness and irritation Nausea with or without vomiting Injection site reaction/inflammation Flushing of face and hands	**Contraindications** Hypersensitivity Caution: Use cautiously in clients who are taking lithium, because concomitant use of calcitonin salmon and lithium may lead to a reduction in plasma lithium concentration due to increased urinary clearance of lithium

TABLE 27.14 **Drug Prototype Table: Calcitonin Salmon** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking calcium preparations, vitamin D, bisphosphonates, calcimimetics, and peptide hormones:

- Monitor calcium, vitamin D, phosphate, PTH, and thyroid hormones closely and report abnormalities to the health care provider.
- Ensure the client is able to sit/stand for 30–60 minutes after the administration of bisphosphonates.
- Educate the client taking calcium preparations, vitamin D, and bisphosphonates to eat foods high in calcium and vitamin D such as spinach, kale, soybeans, salmon, sardines, and fortified dairy products.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a calcium preparation, vitamin D, bisphosphonate, calcimimetic, or peptide hormone should:

- Take the drug exactly as prescribed by the health care provider.
- Report gastrointestinal disturbance, muscle pain, muscle spasms, bone pain, fatigue, or rash to the health care provider because these may be symptoms of a severe reaction.
- Adhere to proper diet involving calcium and vitamin D products as instructed by the health care provider.
- Notify the health care provider if they are pregnant or plan to become pregnant or if they are breastfeeding.
- Store out of reach children and away from heat, moisture, and light.

The client taking a calcium preparation, vitamin D, bisphosphonate, calcimimetic, or peptide hormone *should not:*

- Take over-the-counter medications or herbal supplements without consulting with the health care provider.
- Lay in a supine position for 30–60 minutes after taking a bisphosphonate.

FDA BLACK BOX WARNING

Bisphosphonates

Jaw necrosis and subtrochanteric and diaphyseal femur fractures have been reported in clients treated with bisphosphonates.

Chapter Summary

This chapter focused on a brief introduction to the thyroid and parathyroid glands and their hormones as well as specific thyroid and parathyroid disorders. The structure and function of the thyroid and parathyroid glands were covered, along with diagnostic testing that involves hormones associated with those structure functions. A brief pathophysiology was provided for hypothyroidism, hyperthyroidism, hypoparathyroidism, and hyperparathyroidism. Thyroid, antithyroid, calcium, vitamin D, bisphosphonates, calcimimetics, and peptide hormone drugs were presented and discussed, along with nursing implications and client education.

Key Terms

antithyroid drugs inhibit the thyroid hormone so that the body can maintain normal thyroid homeostasis

bisphosphonates pyrophosphate analogues that inhibit bone resorption and increase bone density

calcimimetics drugs that mimic the action of calcium in the parathyroid glands or other tissues

calcitonin a hormone secreted by the thyroid gland that lowers blood calcium

Chvostek sign a twitch of the facial muscles that occurs with gentle tapping of the cheek and in front of the ear

dihydroxyvitamin D_3 an active form of vitamin D_3 that increases uptake of calcium absorption in the intestine

endocrine glands glands within the endocrine system that release hormones to control processes that occur within the body

goiter an abnormal enlargement of the thyroid gland

Graves' disease an immune disorder that results in the overproduction of thyroid hormones

Hashimoto thyroiditis an autoimmune disorder that involves chronic inflammation of the thyroid gland, resulting in hypothyroidism

iodine a mineral that the body needs to produce thyroid hormones

iodotyrosine an iodo-derivative of tyrosine that acts as an intermediary in the biosynthesis of thyroid hormone

myxedema coma a rare life-threatening condition caused by advanced hypothyroidism that affects the body's temperature, growth, heart rate, and metabolism

organification the biochemical process that takes place in the thyroid gland, involving the incorporation of iodine into thyroglobulin for the production of thyroid hormone

osteoclast a large multinucleated cell responsible for the dissolution and absorption of bone

osteonecrosis the death of bone tissue due to a lack of blood supply

osteoporosis a condition that leads to the loss of bone mass, which thereby weakens bone

Paget's disease a disease that disrupts the body's normal bone recycling process of replacing old bone tissue with new bone tissue

parathyroid hormone (PTH) a peptide hormone secreted by the parathyroid glands that regulates serum calcium within the body

thyroglobulin a protein present in the thyroid gland from which thyroid hormones are synthesized

thyroid drugs drugs that replace the thyroid hormone so that the body can maintain its normal function

thyroid gland a butterfly-shaped gland located in front of the neck below the voice box that is responsible for metabolism and iodine homeostasis within the body

thyroid storm (thyrotoxic crisis) a rare life-threatening condition that occurs when the thyroid gland releases too much thyroid hormone

thyroid-stimulating hormone (TSH) a hormone that stimulates the production of thyroxine and triiodothyronine; also known as thyrotropin

thyroxine (T4) a hormone released by the thyroid gland that contains iodine and that increases the rate of chemical reactions within cells

triiodothyronine (T3) a hormone released by the thyroid gland that plays a role in controlling the body's metabolic rate, heart and digestive functions, muscle control, brain development and function, and bone maintenance

Trousseau sign an involuntary contraction of the muscles in the hand and wrist

Review Questions

1. A nurse is assessing a client with hyperthyroidism. Which clinical manifestation should the nurse anticipate the client will report?
   a. Cold intolerance
   b. Weight gain

c. Frequent mood changes
d. Constipation

2. A nurse is reviewing the laboratory values for a client diagnosed with hypothyroidism. The nurse should expect an elevation in which laboratory value?
a. PTH
b. T3
c. T4
d. TSH

3. A nurse is teaching a client with newly diagnosed hyperthyroidism. For which medication should the nurse provide client education?
a. Desiccated thyroid extract
b. Levothyroxine
c. Liothyronine sodium
d. Methimazole

4. A nurse is teaching a client about levothyroxine for hypothyroidism. The nurse should instruct the client to avoid which food?
a. Grapefruit juice
b. Garlic
c. Soy
d. Sardines

5. A nurse is assessing a client who is receiving levothyroxine for hypothyroidism. Which therapeutic drug response should the nurse anticipate?
a. Decreased appetite
b. Decreased heart rate
c. Increased energy
d. Increased weight

6. Which laboratory findings would indicate to the nurse that a client has hypoparathyroidism?
a. Ionized serum calcium 5.0 mg/dL
b. Total serum calcium 9.8 mg/dL
c. Phosphate 5.7 mg/dL
d. Vitamin D 50 mmol/L

7. A nurse is assessing a client diagnosed with hyperparathyroidism. Which findings should the nurse expect to find?
a. Bone pain
b. Chvostek sign
c. Paresthesia
d. Trousseau sign

8. A nurse is teaching a client diagnosed with osteoporosis secondary to hyperparathyroidism about a new prescription for alendronate. Which adverse effect should the nurse teach the client to report to the health care provider?
a. Dyspepsia
b. Hyperthermia
c. Hypotension
d. Metallic taste

9. The health care provider ordered levothyroxine 0.275 mg once daily for a client with hypothyroidism.

Levothyroxine is available as a 137 mcg tablet. How many tablets will the nurse administer to the client?

a. 1
b. 2
c. 3
d. 4

10. A client with hyperthyroidism has an order for methimazole 15 mg orally daily, in three divided doses. How many milligrams will the nurse administer for each dose?

a. 3 mg
b. 5 mg
c. 7.5 mg
d. 10 mg

CHAPTER 28
Diabetic Drugs

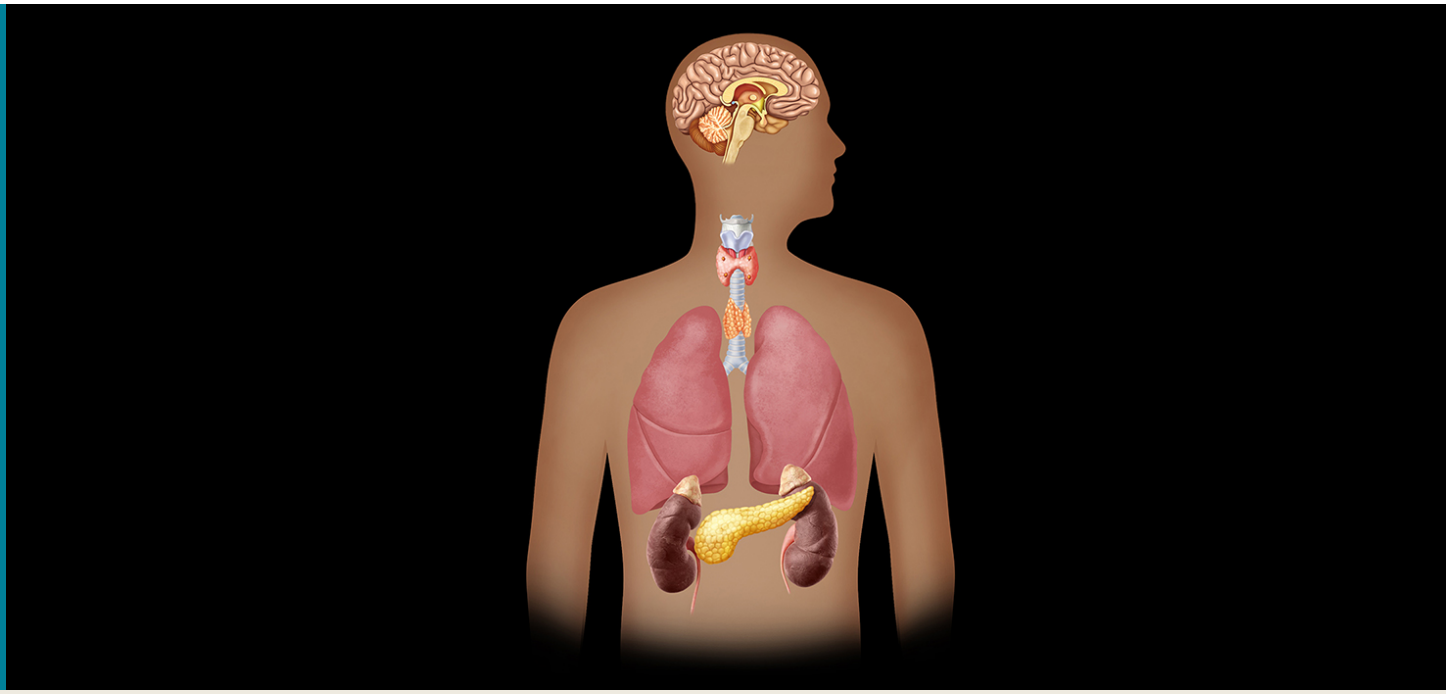


FIGURE 28.1 The endocrine system regulates all biological processes related to development of the brain and nervous system, reproduction, growth, and metabolism. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION **Diabetes** is a long-term chronic health condition that affects millions of people worldwide. It alters how the body regulates glucose from food and uses it for energy. Diabetes affects people of all races, sexes, and ages. According to the Centers for Disease Control and Prevention (CDC, n.d.-a), diabetes and diabetes-related health complications can be serious and costly. The eighth leading cause of death in the United States, diabetes costs a total estimated $327 billion in medical costs and lost work and wages (CDC, n.d.-a). Along with dietary modifications, diabetes management includes **insulin**, **non-insulin injectable diabetes drugs**, and **oral diabetes drugs**. This chapter will explore diabetes and the pharmacologic and non-pharmacologic treatments for this disease process.

28.1 Introduction to Diabetes

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 28.1.1 Describe the pathophysiology of type 1 and type 2 diabetes.
- 28.1.2 Identify clinical manifestations of diabetes.
- 28.1.3 Identify the etiology and diagnostic studies related to diabetes.

The islets of Langerhans are clusters of cells located in the pancreas. They are composed of alpha and beta cells, which are crucial for glucose homeostasis. Alpha (α) cells produce glucagon, which breaks down glycogen into glucose in the liver. Beta (β) cells secrete insulin, which regulates glucose metabolism and facilitates absorption of glucose from the bloodstream into cells (see Figure 28.2). Diabetes mellitus is a metabolic disease that is

characterized by hyperglycemia associated with alterations in carbohydrate, protein, and fat metabolism (Dilworth et al., 2021).

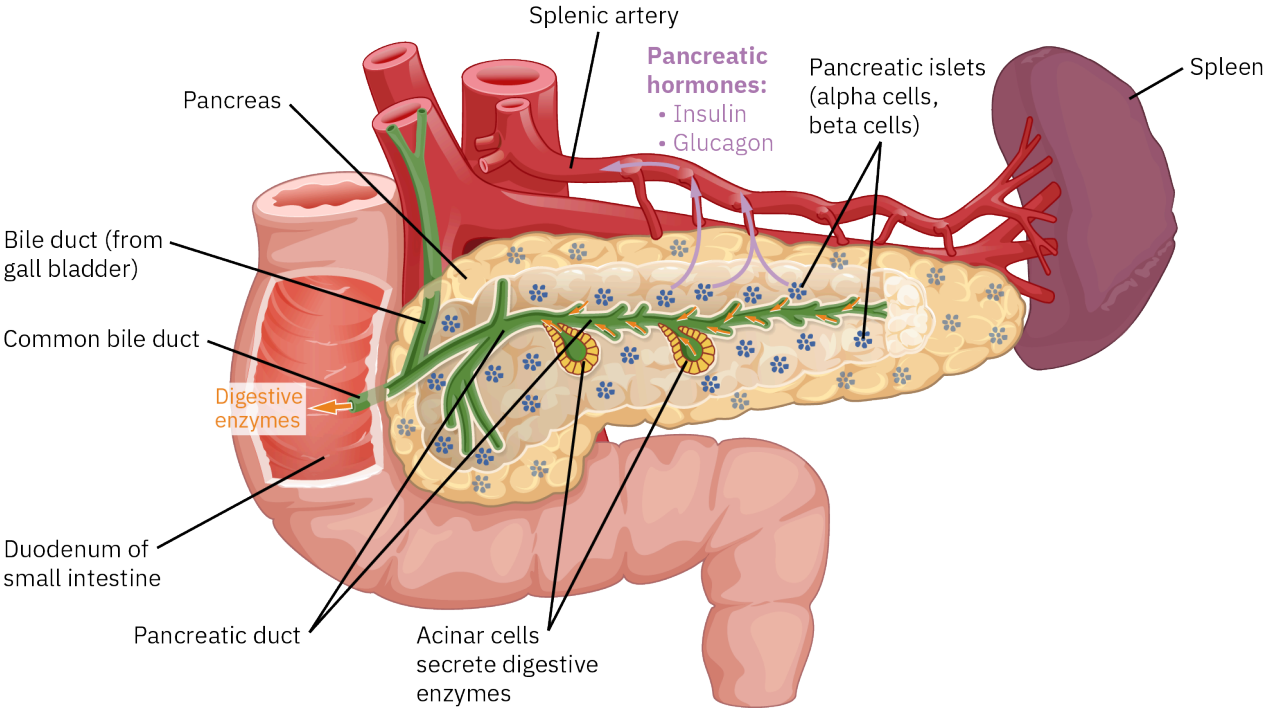


FIGURE 28.2 The primary function of the pancreas is to maintain blood sugar homeostasis within the body by producing glucagon, insulin, and other hormones. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Type 1 Diabetes

Type 1 diabetes is an autoimmune disorder that causes the body's immune system to attack and destroy the β cells in the pancreas that make insulin. As a consequence, the pancreas stops making insulin. Without insulin, glucose homeostasis is disrupted, resulting in glucose not being able to get into the cells of the body, thus causing elevated glucose levels in the blood. Because the body is destroying the β cells in the pancreas, clients with type 1 diabetes will need to take insulin for the rest of their lives to survive (Holt et al., 2021).

TRENDING TODAY

Type 1 Diabetes and Lantidra

The U.S. Food and Drug Administration (2023) approved Lantidra (donislecel-jujn) (https://openstax.org/r/fdagovnewsevents), the first allogeneic (donor) pancreatic islet cellular therapy made from deceased donor pancreatic cells to treat type 1 diabetes. Lantidra is approved for the treatment of adults with type 1 diabetes who are unable to approach target glycated hemoglobin (average blood glucose levels) because of current repeated episodes of severe hypoglycemia (low blood sugar) despite intensive diabetes management and education.

According to the Centers for Disease Control and Prevention (n.d.-a), 1.6 million U.S. adults aged 20 years or older have type 1 diabetes. The onset of symptoms with type 1 diabetes is often sudden. It typically appears in adolescents and young adults but can occur in childhood as well. Symptoms of type 1 diabetes can be severe, and the disease process can be difficult to control. Risk factors include family history and age. White clients are more likely to develop type 1 diabetes than Black, Asian American, Hispanic, or Latino/Latina clients (CDC, 2022b).

Type 2 Diabetes

Type 2 diabetes occurs when the pancreas does not produce enough insulin or the body is not using insulin effectively. Figure 28.2 shows the mechanism of normal blood sugar absorption versus insulin resistance with type

2 diabetes. The β cells in the pancreas continue to have some degree of functionality with varying amounts of insulin secretion, resulting in elevated blood glucose levels and insulin resistance. Type 2 diabetes may be managed with healthy eating and being active, or the health care provider may prescribe insulin, other injectable medications, or oral diabetic medicines to help clients manage blood sugar and avoid complications (CDC, n.d.-b).

The Centers for Disease Control and Prevention (n.d.-b) reported that of the approximately 37 million U.S. adults who have diabetes, approximately 90%–95% of them have type 2 diabetes. Unlike type 1 diabetes, type 2 diabetes symptoms are gradual in onset. The disease typically appears in people over age 45; however, it is becoming more common in children, adolescents, and young adults. Risk factors include having prediabetes, obesity, age 45 or older, family history, sedentary lifestyle, fatty liver, and a history of gestational diabetes. Black, Alaska Native, American Indian, Hispanic, and Latino/Latina people are more likely to develop type 2 diabetes (CDC, 2022b).

Gestational Diabetes

Gestational diabetes is a type of diabetes that can develop during pregnancy in clients who do not already have diabetes. Testing for gestational diabetes usually occurs between 24 and 28 weeks of pregnancy (NIH, n.d.). Gestational diabetes causes high blood glucose levels that can affect the pregnancy and the fetus. Symptoms are usually unnoticeable; however, the client may exhibit signs of increased thirst and increased urination. Gestational diabetes is controlled with dietary management and exercise. Pharmacologic methods are incorporated only if the disease process is unmanageable with diet and exercise and only introduced if safe for both the pregnant person and the fetus. Blood sugar levels typically return to baseline soon after the delivery of the newborn. Clients with gestational diabetes are at a higher risk of developing type 2 diabetes as they age (American Diabetes Association, n.d.-a).

Complications of Diabetes

Complications from diabetes can affect all body systems. They include cerebrovascular disease, cardiovascular disease, diabetic neuropathy, diabetic retinopathy, cataracts, glaucoma, periodontal disease, peripheral vascular disease, foot damage, stroke, increased risk of infection, and poor wound healing.

Prevention

There is no known way to prevent type 1 diabetes. Type 2 diabetes can be prevented with lifestyle modifications such as diet, exercise, weight loss, and developing a diabetes prevention program with the health care provider (American Diabetes Association, n.d.-a).

Clinical Manifestations of Diabetes

Typical clinical manifestations of diabetes include polyuria (increased urination), polydipsia (increased thirst), weight loss without trying, blurry vision or vision changes, paresthesia (tingling in the feet and hands), dry skin, and fatigue (see Figure 28.3). Hypoglycemia and hyperglycemia play a role in diabetes management and are discussed in the following sections.

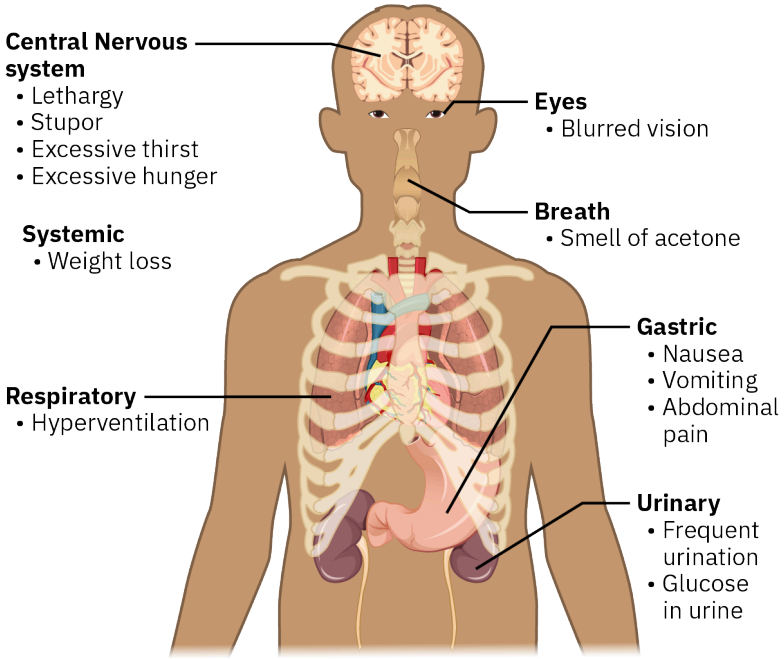


FIGURE 28.3 There are a number of clinical manifestations of diabetes affecting the respiratory, gastric, urinary, and central nervous system. (credit: modification of work "Main symptoms of diabetes" by Mikael Häggström, used with permission/Wikimedia Commons, Public Domain)

Hypoglycemia

Hypoglycemia occurs when the blood glucose level in the body falls below the normal range. The expected values for normal fasting blood glucose concentration are between 70 mg/dL and 100 mg/dL (World Health Organization [WHO], n.d.). When blood glucose levels are too low, the brain does not get enough glucose to function, which in its most severe form can cause coma and death. Signs and symptoms of hypoglycemia include feeling shaky, sweating/chills, clammy skin, dizziness/feeling faint, agitation, confusion, blurred or impaired vision, slurred speech, and tachycardia/bradycardia (American Diabetes Association, n.d.-c).

Treatment of hypoglycemia includes the "15–15 rule": 15 grams of carbohydrates to raise the blood glucose level and a blood glucose monitoring check 15 minutes after administration of the carbohydrates. If the blood glucose level remains under 70 mg/dL, then glucose tablets or 15 grams of carbohydrates may be repeated until the blood glucose is at least 70 mg/dL. Glucagon may be used to treat clients with diabetes when their blood glucose is too low to treat using the 15–15 rule (American Diabetes Association, n.d.-c). Glucagon can be given intravenously, intramuscularly, or subcutaneously if the client is unable to eat or drink or if the client is unconscious.

Hyperglycemia

Hyperglycemia occurs when the blood glucose level in the body is above the normal range and the body has too little insulin or is too insulin resistant to lower the blood glucose level on its own. This causes a disruption in glucose homeostasis. If a blood glucose level is above 110 mg/dL, it is considered hyperglycemia. Symptoms vary per individual. Some clients may have mild symptoms with blood glucose levels between 110 mg/dL and 240 mg/dL. Severe symptoms can result in diabetic **ketoacidosis**, coma, and death. Signs and symptoms of hyperglycemia include frequent urination (**polyuria**), increased thirst (**polydipsia**), increased hunger (**polyphagia**), blurred vision, restlessness, unintentional weight loss, abdominal pain, vomiting, drowsiness, hot/dry skin, hypotension, and coma (American Diabetes Association, n.d.-b; Sapra & Bhandari, 2023).

Treatment of hyperglycemia can be as simple as dietary management and exercise if blood glucose levels are 110–240 mg/dL. However, if increasing fluid intake, diet, and exercise does not lower blood glucose levels, the individual will require an oral diabetes agent, insulin, and/or a non-insulin injectable drug to lower the blood glucose levels (American Diabetes Association, n.d.-b; Feingold, 2022).

LINK TO LEARNING

Race and Diabetes Risk

Access multimedia content (https://openstax.org/books/pharmacology/pages/28-1-introduction-to-diabetes)
In this video, Dr. Margrethe Horlyck-Romanovsky discusses intra-ethnic diabetes disparities and how to improve diabetes risk assessments for diverse populations. She also discusses the ways in which immigrant status, ethnicity, and race can influence diabetes risk in populations of African descent.

Diagnostic Testing for Diabetes

There are several diagnostic tests to determine if a person has diabetes. Health care providers will typically use one or more of the following tests to determine if an individual has diabetes.

Glycosylated Hemoglobin (A1c or HbA1c)

A **glycosylated hemoglobin (A1c)** test, also known as a hemoglobin A1c or HbA1c test, measures the blood sugar level over the past 90 days. It determines the amount of hemoglobin proteins that are coated with glucose. A HbA1c below 5.7% is normal. A HbA1c between 5.7% and 6.4% represents prediabetes, and a level of 6.5% or higher indicates diabetes (American Diabetes Association, n.d.-a).

Fasting Blood Glucose

A **fasting blood glucose** test measures the blood sugar level after an overnight fasting period. A fasting blood glucose level of 99 mg/dL or lower is normal, 100–125 mg/dL indicates prediabetes, and 126 mg/dL or higher indicates diabetes (American Diabetes Association, n.d.-a).

Random Blood Glucose

A **random blood glucose** test measures the blood sugar level at the time tested. This test can be taken at any time of the day, and the individual being tested does not need to fast. A blood sugar level of 200 mg/dL or higher indicates diabetes (American Diabetes Association, n.d.a).

Comorbidity Tests

Diabetes impacts multiple systems within the body. The health care provider may order additional testing to determine the impact of diabetes on other body systems. These diagnostic tests will not determine if a client has diabetes; however, they will help show how diabetes is impacting other systems. Typical diagnostic testing includes complete blood cell count, basic metabolic panel, chest x-ray, echocardiogram, electrocardiogram, electromyography, and other radiologic tests such as a computed tomography (CT) scan or magnetic resonance imaging (MRI).

TRENDING TODAY

Prediabetes

More than one in three U.S. adults have prediabetes. As defined by the CDC, “a person with prediabetes has a blood sugar level higher than normal, but not high enough for a diagnosis of diabetes. He or she is at higher risk for developing type 2 diabetes and other serious health problems, including heart disease and stroke” (Alvarez et al., 2023). To better address the growing numbers and problems associated with prediabetes and diabetes, U.S. Congress authorized the CDC to implement the National Diabetes Prevention Program. This program provides individuals with guidance regarding diabetes and lifestyle changes to reduce the risk of developing type 2 diabetes and to better manage the disease process for those who already have type 2 diabetes.

Access multimedia content (https://openstax.org/books/pharmacology/pages/28-1-introduction-to-diabetes)
Watch the video “Changing Lifestyles to Prevent Type 2 Diabetes,” which discusses how diabetes is a public health crisis, the prevention program, and reducing risks for serious complications as a result of diabetes.

Visit the National Diabetes Prevention Program website (https://openstax.org/r/coveragetoolkitorg) to learn more about key milestones, research conducted, and why the program was authorized. This website gives an overview

of the National Diabetes Prevention Program and provides valuable information for those with prediabetes and type 2 diabetes.

UNFOLDING CASE STUDY

Part A

Read the following clinical scenario to answer the questions that follow. This case will evolve throughout the chapter.

Alaina Sanders is a 65-year-old client who presented to her health care provider's office reporting fatigue, an increase in urination, feeling thirsty all the time, and blurred vision for the past 3 months.

History

Hyperlipidemia
Hypertension
Does not exercise or follow a special diet

Current Medications

Atorvastatin 20 mg once daily
Amlodipine 10 mg once daily

Vital Signs		Physical Examination
Temperature:	97.8°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention or peripheral edema noted. S1, S2 heard on auscultation. • *Respiratory:* Clear to auscultation bilaterally • *GI:* Abdomen soft, nontender, nondistended • *GU:* See history of present illness (HPI) • *Neurological:* Within normal limits • *Integumentary:* No wounds noted. Skin appropriate for age.
Blood pressure:	102/74 mm Hg	
Heart rate:	78 beats/min	
Respiratory rate:	20 breaths/min	
Oxygen saturation:	95% on room air	
Height:	5'5"	
Weight:	188 lb	

TABLE 28.1

1. After reviewing the client's symptoms, the nurse anticipates which diagnosis by the health care provider?
   a. Gestational diabetes
   b. Type 1 diabetes
   c. Type 2 diabetes
   d. Hypoglycemia

2. To determine the client's blood glucose level over the last 3 months, which diagnostic test does the nurse anticipate the health care provider will order?
   a. Complete blood count
   b. Random blood glucose
   c. Fasting blood glucose
   d. Glycosylated hemoglobin (hemoglobin A1c)

28.2 Insulin and Non-Insulin Injectable Diabetes Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 28.2.1 Identify the characteristics of insulin and non-insulin injectable drugs used to treat diabetes.
- 28.2.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of insulin and non-insulin injectable drugs used to treat diabetes.
- 28.2.3 Describe nursing implications of insulin and non-insulin injectable drugs used to treat diabetes.
- 28.2.4 Explain the client education related to insulin and non-insulin injectable drugs used to treat diabetes.

Insulin

Insulin is released by ß cells from the islets of Langerhans in the pancreas after eating a meal. The carbohydrates from the meal are broken down into glucose. As glucose enters the bloodstream, insulin is secreted and allows the cells in muscles, fat, and the liver to absorb the glucose for energy (American Diabetes Association, n.d.-d). Insulin not only is important for glucose homeostasis, but it also plays a role in lipid metabolism through lipolysis and assists in protein metabolism through downregulation of hepatic and muscle enzymes, and its action within endothelial cells and macrophages has an anti-inflammatory effect on the body.

Insulin has three characteristics: onset, peak, and duration. Onset is the length of time before insulin reaches the bloodstream and begins to lower glucose levels. Peak time is discussed below. Duration is how long insulin continues to lower blood glucose levels.

Peak Time

Peak time is when insulin is at its maximum strength in terms of lowering blood glucose levels. Individuals are at a higher risk of developing hypoglycemia symptoms when insulin is peaking (American Diabetes Association, n.d.-d).

Types of Insulin

There are different types of insulin based on the client's needs. In this chapter, rapid-acting, short-acting, intermediate-acting, and long-acting insulins, as well as premixed insulins, will be discussed. Insulins are typically clear except for insulin isophane NPH, which is cloudy.

SAFETY ALERT

Insulin-Independent Double Checks

- Double-check to ensure the correct type of insulin is being administered, especially if the client is taking more than one type of insulin. Perform independent double checks on the vial and dose of insulin.
- Only use insulin syringes to administer insulin.
- Double-check client identifiers, type, product, dose, and measured dose of insulin prior to administering the drug to the client to decrease the risk of medication error.

(Source: Institute for Safe Medication Practices, 2019).

Rapid-Acting Insulin

Rapid-acting insulin begins to work approximately 15–30 minutes after injection. It peaks in 1–2 hours after injection, and its duration is 2–4 hours. Insulin aspart (Novolog), insulin glulisine (Apidra), and insulin lispro (Humalog) are rapid-acting insulins (DailyMed, *Novolog*, 2021; DailyMed *Apidra*, 2023; DailyMed, *Humalog*, 2022).

Short-Acting Insulin

Short-acting insulin, also known as regular insulin, begins to work within 30 minutes to 1 hour after injection. It peaks in 2–3 hours after injection, and its duration is 3–6 hours. Human regular insulin (Humulin R and Novolin R) is a short-acting insulin (DailyMed, *Humulin R*, 2023; DailyMed, *Novolin R*, 2022).

Intermediate-Acting Insulin

Intermediate-acting insulin begins to work 2–4 hours after injection. It peaks in 4–12 hours, and its duration is 12–18 hours. Insulin isophane NPH (Humulin N and Novolin N) is a type of intermediate-acting insulin (DailyMed,

Humulin N, 2023; DailyMed, *Novolin N*, 2022).

Long-Acting Insulin

Long-acting insulin begins to work 1–2 hours after injection. It has no peak time and acts to lower blood glucose levels up to 24 hours. Insulin degludec (Tresiba), insulin detemir (Levemir), and insulin glargine (Lantus) are long-acting insulins (DailyMed, *Tresiba*, 2022; DailyMed, *Lantus*, 2022).

Premixed Insulin

Premixed insulin combines intermediate- and short-acting insulin into a single injection. These injections are usually taken 10 to 30 minutes before breakfast and dinner to provide both basal and mealtime coverage.

Table 28.2 lists common insulins and their actions.

Drug	Onset	Peak	Duration	Method
Rapid-acting insulin Insulin aspart (Novolog) Insulin glulisine (Apidra) Insulin lispro (Humalog)	15–30 minutes	1–2 hours	2–4 hours	Take 15 minutes before a meal or immediately after a meal. Often used with a longer-acting insulin.
Short-acting insulin Human regular insulin (Humulin R, Novolin R)	30 minutes–1 hour	2–3 hours	3–6 hours	Take 30–60 minutes before a meal. May be used with a longer-acting insulin.
Intermediate-acting insulin Insulin isophane NPH (Humulin N, Novolin N)	2–4 hours	4–12 hours	12–18 hours	Covers insulin needs for 12 hours or longer, or overnight. Often used with a rapid- or short-acting insulin.
Long-acting insulin Insulin degludec (Tresiba) Insulin detemir (Levemir) Insulin glargine (Lantus)	1–2 hours	Does not peak	Up to 24 hours	Covers insulin needs for approximately an entire day. Often used with a rapid- or short-acting insulin.

TABLE 28.2 **Types of Insulin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Administration of Insulin

Insulin typically comes as an injectable source because it needs to bypass the first pass of digestion for absorbtion due to its instability in the presence of gastric acid. Insulin is injected into the **subcutaneous** tissue via an insulin syringe, insulin pen, or insulin pump. Injection sites for insulin are located primarily on the abdomen, back of the upper arm, lower back, buttocks, and upper outer thigh (see Figure 28.4). The rate of absorption depends on the injection site. Insulin injection sites should be rotated to prevent fatty deposits and site irritation (American Diabetes Association, n.d.-d).

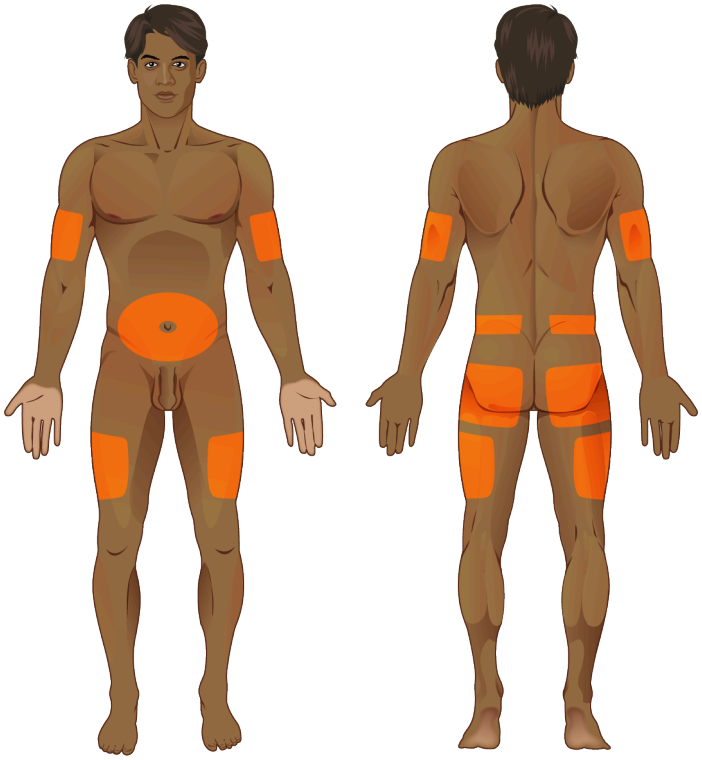


FIGURE 28.4 The most common insulin injection sites are upper outer arms, abdomen, upper outer thighs, and the buttocks. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Methods of Insulin Dosing

Most insulin is given on a carbohydrate-to-insulin ratio via a fixed-dose insulin method with an insulin syringe (American Diabetes Association, n.d.-d). Fixed-dose therapy can apply to clients who take one injection a day and to clients taking multiple injections per day. With fixed-dose insulin therapy, a client will take the same amount of insulin at a specific time each day; for example, take 30 units of insulin at breakfast each day and 20 units at dinner each day. Because the doses stay the same from one day to another, the client will need to eat a specific amount of carbohydrates for each meal (Diabetes.co.uk, 2023).

In health care settings such as a hospital or a nursing home, insulin may also be administered via a **sliding scale coverage** method. The sliding scale method typically uses a short-acting insulin (Migdal et al., 2021). The dose of insulin is based on the blood glucose level just before a meal, which is taken using a glucometer.

Although still commonly used in health care settings, sliding scale insulin has become controversial in recent years because it has not been shown to control blood glucose levels very well. Sliding scale insulin dosing not only has demonstrated poor blood glucose control, but also does not reflect a person's current insulin needs based on their diet, weight, and insulin history. Currently, it is recommended that **basal insulin dosing** be used instead of sliding scale for glycemic control. With basal dosing, a long-acting insulin is administered to keep insulin levels steady throughout the day, and then a rapid-acting insulin is administered during mealtimes to regulate spikes in blood glucose levels after meals (Migdal et al., 2021).

Insulin Pen

An **insulin pen** is a pen-shaped injector device that combines insulin and a syringe in one unit. Insulin pens are prefilled with an insulin cartridge or have a prefilled insulin reservoir. The pens have a dial, and disposable needles can be attached to the pen. Insulin pens are relatively easy to use and convenient. To use an insulin pen, the client should twist on a needle, dial the dose as prescribed by the health care provider, and inject into the subcutaneous site. The needle is then thrown away into a sharps container, and the pen is placed in a safe area until the next dose of insulin is due (American Diabetes Association, n.d.-d).

Pens are disposable after all of the insulin in the pen has been used or the pen has expired. Pens are often color-coded to make it easier to recognize the type of insulin the pen contains. Pens are portable and can be used discreetly in public places when needed (American Diabetes Association, n.d.-d).

CLINICAL TIP

Insulin Pens

Insulin pens should never be used for more than one person or for someone other than the person they were prescribed for. Regurgitation of blood into the insulin cartridge or reservoir can occur after injection. The risk of blood-borne pathogen transmission increases if the insulin pen is used on more than one person (CDC, 2022a).

Insulin Pump and Continuous Glucose Monitoring

An **insulin pump** is a small, computerized infusion set device that delivers insulin. Doses of a rapid-acting insulin are supplied through a flexible catheter that has been inserted through the skin into the subcutaneous tissue. Insulin pumps are often integrated with a **continuous glucose monitor (CGM)**, which is a device that monitors blood glucose levels on a continual basis. CGMs decrease the need for finger sticks and blood sampling with a glucometer. CGMs are applied to the back of the arm, abdomen, or upper gluteal areas and covered with a bandage. These devices need to be changed every 10–14 days. CGMs are accompanied by an app that synchronizes with the sensor in the device. This allows for easy and portable blood glucose tracking. Insulin pumps and CGMs have been successfully utilized across all age groups (American Diabetes Association, n.d.-d).

Insulin pumps are set to deliver a small dose of insulin continuously. This is called a basal dose insulin, and it mimics the body's normal release of insulin. The basal dose insulin is calculated and programmed by the health care provider based on the client's glycemic needs. A **bolus** dose insulin may also be delivered by the insulin pump close to mealtimes to control the rise in blood glucose levels after a meal (American Diabetes Association, n.d.-d).

LINK TO LEARNING

Insulin Pumps (https://openstax.org/r/clevelandclinicorg)

The Cleveland Clinic presents information on insulin pumps, reasons they are used, and how to wear an insulin pump. It provides a video on insulin pumps as well as information on risks and benefits.

Intravenous Insulin

Intravenous insulin is administered by a health care professional to a client in a health care setting. Insulin is administered directly into the bloodstream via an intravenous catheter. Intravenous insulin is used to treat hyperglycemic emergencies and other conditions such as diabetic ketoacidosis, hyperosmolar (extremely high glucose) states, and hyperkalemia. Human regular insulin is typically the only insulin given intravenously; however, according to Rubin, Khanna, and McIver (2022), insulin aspart, a rapid-acting insulin, may be administered through a subcutaneous infusion via pump or intravenously as a diluted solution with close monitoring of blood glucose and serum potassium levels. Once the insulin is injected into the intravenous catheter, it only takes a few minutes for it to enter the bloodstream and to start working to lower blood glucose levels. Intravenous insulin therapy is typically administered short term for a period of 3–12 hours and requires close monitoring by a health care professional (Thota & Akbar, 2022).

Intravenous insulin can be administered via a bolus dose method and/or as a **titrated** insulin drip requiring an infusion device. A bolus dose of insulin is administered via the intravenous line when rapid reduction of blood glucose levels is needed, such as with a severe hyperglycemic state like diabetic ketoacidosis (Dhatariya et al., 2020).

A titrated intravenous insulin drip, also called an insulin infusion, may be required to assist with reducing severely elevated blood glucose levels when a bolus dose of intravenous insulin alone does not assist in reaching the targeted blood glucose level for the client. Titrated insulin drips provide 1 unit of a rapid-acting or short-acting insulin per milliliter of 0.9% sodium chloride. The titrated insulin drips are typically started at 1 unit/hour and titrated based on the facility's protocol in association with the client's blood glucose level. For example, if the client's blood glucose level is 111–140 mg/dL, the titrated insulin drip is set to infuse at 1 unit/hour; if the client's blood glucose level is 141–175 mg/dL, the titrated insulin drip is set to infuse at 2 units/hour. Blood glucose levels are checked hourly, and the insulin infusion is titrated based on the blood glucose levels until the client reaches

glucose homeostasis. Once the client has reached glucose homeostasis, subcutaneous insulin is administered, and the client is weaned off of the titrated insulin drip (Dhatariya et al., 2020).

CLINICAL TIP

Titrate Insulin Drip to Subcutaneous Insulin

The nurse or health care provider should check blood glucose levels 1 hour prior to discontinuing the titrated insulin drip. The first dose of subcutaneous insulin should be administered prior to discontinuing the titrated insulin drip. The titrated insulin drip should be continued for 30–60 minutes after the subcutaneous insulin injection to prevent rebound hyperglycemia (Dhatariya et al., 2020).

Adverse Effects and Contraindications

Insulin is a natural hormone present in the body. In clients with diabetes, insulin use as a medication is generally safe and effective; however, there can be certain adverse effects and contraindications associated with its use.

Typical adverse effects of all types of insulin include hypoglycemia (symptoms include shakiness, dizziness, sweating, confusion, and, in severe cases, loss of consciousness), weight gain (due to an increased glucose uptake and storage in cells), injection site reactions (such as redness, swelling, or itching), lipodystrophy (fat tissue changes from repeated use of the same injection site), and fluid retention (swelling in the legs and feet).

Contraindications include hypersensitivity to the components in the insulin, especially animal-derived insulins. Caution should be used in clients with medical conditions that cause fluid retention, such as heart failure and renal failure (as insulin can cause additional fluid retention leading to volume overload), and in clients with liver failure (as insulin is metabolized by the liver).

Table 28.3 is a drug prototype table for the diabetes drug insulin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Insulin **Mechanism of Action** Lowers the level of glucose in the blood and provides cells with glucose for energy by helping cells to absorb glucose	**Drug Dosage** Varies based on client's glycemic need, blood glucose levels, and health status.
Indications Hyperglycemia Glucose homeostasis **Therapeutic Effects** Lowers blood glucose levels Promotes use of glucose by cells	**Drug Interactions** Alcohol **Food Interactions** No significant interactions
Adverse Effects Weakness Headache Nausea/diarrhea/abdominal pain Cough Weight gain/edema Injection site irritation and reaction Lipodystrophy	**Contraindications** Hypoglycemia Caution: Monitor closely for signs of hypoglycemic reaction during insulin peak time

TABLE 28.3 **Drug Prototype Table: Insulin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Non-Insulin Injectable Drugs

Non-insulin injectable drugs provide an alternative to insulin therapy for clients with diabetes. They act on

hormones that are secreted along with insulin by the pancreas to control glucose homeostasis. These drugs were first approved for use in the United States in 2005 (Feingold, 2022; Campbell, 2021).

Amylin Analogs

Amylin is a hormone secreted along with insulin by the pancreas in response to food intake. In 2005, pramlintide (Symlin) was the first FDA-approved amylin analog non-insulin injectable drug. This drug can be used for clients with diabetes who are taking insulin. Pramlintide slows gastric emptying and blocks the release of glucagon from the liver after a meal. This drug is administered before mealtimes. Adverse effects include nausea, loss of appetite, fatigue, headache, and weight loss. It is contraindicated in clients with hypersensitivity to amylin analogs or who have hypoglycemia or gastroparesis (Maikawa et al., 2020; Campbell, 2021).

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

GLP-1 receptor agonists are a class of non-insulin injectable drugs that impact the gut hormone incretin, which works to increase insulin secretion in response to meals. These drugs help the pancreas release insulin after eating, limit glucagon, and slow down digestion. GLP-1 receptor agonists are approved for type 2 diabetes treatment. They have not yet been approved for type 1 diabetes management. Adverse effects include nausea, vomiting, diarrhea, abdominal discomfort, and loss of appetite. Contraindications include hypersensitivity to GLP-1 receptor agonists, medullary thyroid carcinoma, and multiple endocrine neoplasia (Feingold, 2022).

CLINICAL TIP

GLP-1 Receptor Agonists

Hypoglycemic reactions are greater when GLP-1 receptor agonists are used with sulfonylureas and insulin. Clients should be monitored closely for signs of hypoglycemia (Feingold, 2022).

Dulaglutide

Dulaglutide (Trulicity) is taken once a week at any time of day, with or without food. It can be used in combination with sulfonylureas, non-sulfonylurea biguanides, thiazolidinediones, and insulin. Adverse effects include nausea, diarrhea, vomiting, abdominal pain, decreased appetite, indigestion, fatigue, and weight loss (Jódar et al., 2022).

Exenatide

Exenatide (Byetta) is taken twice a day, 1–2 hours before a meal. It can be used in combination with sulfonylureas, non-sulfonylureas biguanides, thiazolidinediones, and insulin. Adverse effects include nausea, vomiting, decreased appetite, and weight loss (Wysham et al., 2020).

Exenatide extended release (Bydureon) is taken once every 7 days. It can be used in combination with sulfonylureas, non-sulfonylureas biguanides, and thiazolidinediones. It should not be administered with exenatide (Byetta) or used in combination with insulin. Adverse effects include nausea, vomiting, decreased appetite, and weight loss (Wysham et al., 2020).

Liraglutide

Liraglutide (Victoza) is taken once a day at any time of the day regardless of mealtimes. It can be used in combination with sulfonylureas, non-sulfonylureas biguanides, and thiazolidinediones. Adverse effects include headache, nausea, diarrhea, decreased appetite, and weight loss (He et al., 2019).

Tirzepatide

Tirzepatide (Mounjaro) is taken once a week at any time of day, with or without meals. Adverse effects include nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain (DailyMed, *Mounjaro*, 2023).

Semaglutide

Semaglutide (Ozempic) is taken once a week at any time of the day regardless of mealtimes. It can be used in combination with sulfonylureas, non-sulfonylureas biguanides, thiazolidinediones, and insulin. Adverse effects include nausea, diarrhea, abdominal pain, decreased appetite, weight loss, and constipation (Smits & Van Raalte, 2021).

Table 28.4 lists common non-insulin injectable drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Pramlintide (Symlin)	*Type 1 diabetes:* 15 mcg subcutaneously before major meals. Increase in 15 mcg increments to a maximum pre-meal dose of 30–60 mcg. *Type 2 diabetes:* 60 mcg subcutaneously before major meals, then increase to 120 mcg before meals as tolerated. Wait at least 3 days between dose titrations to minimize nausea.
Dulaglutide (Trulicity)	0.75 mg subcutaneously once weekly. Increase dosage by 1.5 mg increments after at least 4 weeks. Maximum dose: 4.5 mg subcutaneously once weekly.
Exenatide (Byetta, Bydureon)	5 mcg subcutaneously within 60 minutes prior to morning and evening meals at least 6 hours apart. Increase to 10 mcg twice daily after 1 month based on clinical response.
Liraglutide (Victoza)	0.6 mg subcutaneously daily for one week, then increase to 1.2 mg daily. Maximum dose: 1.8 mg daily.
Tirzepatide (Mounjaro)	Initial dose: 2.5 mg injected subcutaneously once weekly. After 4 weeks, increase the dosage to 5 mg injected subcutaneously once weekly. If additional glycemic control is needed, increase the dosage in 2.5 mg increments after at least 4 weeks on the current dose. Maximum dose: 15 mg injected subcutaneously once weekly.
Semaglutide (Ozempic)	0.25 mg subcutaneously once weekly; after 4 weeks increase to 0.5 mg once weekly. Maximum dose: 2 mg once weekly. Wait 5 days between dose titrations.

TABLE 28.4 **Drug Emphasis Table: Non-insulin Injectables** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of amylin analogs include hypoglycemic symptoms (shakiness, dizziness, sweating, confusion, and, in severe cases, loss of consciousness), gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain, and loss of appetite), and injection site reactions.

Contraindications include hypersensitivity to the drug or any of its components and in clients with medullary thyroid cancer and multiple endocrine neoplasia (as these drugs can exacerbate these conditions). Caution should be used in clients with gastroparesis as amylin analogs may further slow down gastric emptying, in clients with severe renal impairment as the drugs are excreted in the urine and can further impair renal function, and in clients with hepatic insufficiency due to the drugs being metabolized by the liver and thus can impede liver functioning.

Table 28.5 is a drug prototype table for non-insulin injectable drugs featuring dulaglutide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Glucagon-like peptide (GLP-1) receptor agonist **Mechanism of Action** Increases insulin secretion when glucose levels are elevated, decreases glucagon secretion, and delays gastric emptying in an effort to lower postprandial glucose levels	**Drug Dosage** 0.75 mg subcutaneously once weekly. Increase dosage by 1.5 mg increments after at least 4 weeks. Maximum dose: 4.5 mg subcutaneously once weekly.
Indications As an adjunct to diet and exercise to improve glycemic control in individuals older than 10 years of age To reduce the risk of major cardiovascular events in adults with type 2 diabetes who have established cardiovascular disease or multiple cardiovascular risk factors **Therapeutic Effects** Lowers postprandial glucose levels	**Drug Interactions** Delays gastric emptying and has the potential to reduce the rate of absorption of concomitantly administered oral drugs **Food Interactions** No significant interactions
Adverse Effects Nausea Vomiting Diarrhea Abdominal pain Decreased appetite	**Contraindications** Medullary thyroid carcinoma Multiple endocrine neoplasia Hypersensitivity Caution: Thyroid C cell tumors Pancreatitis Hypoglycemia Aute kidney injury Severe gastrointestinal disease Diabetic retinopathy Acute gallbladder disease

TABLE 28.5 **Drug Prototype Table: Dulaglutide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking insulin and non-insulin injectable diabetes drugs:

- Assess the client's knowledge about diabetes, signs and symptoms, and treatment and clarify any gaps in knowledge.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Refer client to social services for obstacles in obtaining prescribed drugs, test strips, or a glucometer.
- Provide client teaching regarding the drug, how to administer an injection, and when to call the health care provider. See below for client teaching.

CLIENT TEACHING GUIDELINES

The client using an insulin or non-insulin injectable diabetes drug should:

- Report symptoms of hypoglycemia such as headache, nervousness, sweating, clammy skin, tremor, and tachycardia.
- Report symptoms of hyperglycemia such as increased thirst, increased urine output, hot/dry skin, and sweet, fruity breath odor.
- Keep 15 grams of carbohydrates on hand in case of a hypoglycemic reaction. Orange juice, graham crackers, and hard candy are appropriate carbohydrate choices during hypoglycemia.

- Show family members and their support system how to administer glucagon during a hypoglycemic reaction if the client cannot eat or drink or is unconscious.
- Store insulin in a refrigerator at approximately 36–46°F.
- Store non-insulin injectables per manufacturer's packaging.
- Ask the health care provider prior to taking any OTC drugs or herbal supplements with insulin and non-insulin injectables because they may increase the risk of hypoglycemia or hyperglycemia.
- Keep a blood glucose journal for tracking blood glucose levels.
- Rotate insulin injection sites to prevent fatty deposits and injection site reactions.
- Eat an appropriate diet as prescribed and as scheduled with their insulin routine.
- Use safety with injectable syringes and needles and dispose of them properly.

FDA BLACK BOX WARNING

GLP-1 Receptor Agonists

GLP-1 receptor agonists should not be taken if a client has a history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2.

28.3 Oral Antidiabetic Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 28.3.1 Identify the characteristics of oral diabetes drugs.
- 28.3.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of oral diabetes drugs.
- 28.3.3 Describe nursing implications of oral diabetes drugs.
- 28.3.4 Explain the client education related to oral diabetes drugs.

Oral diabetes drugs are used to treat type 2 diabetes. They are ineffective with type 1 diabetes because type 1 diabetic β cells are not functioning. These drugs lower blood glucose levels in various ways, such as stimulating insulin production from β cells, decreasing insulin resistance, slowing glucose absorption from the gastrointestinal tract, and altering the release of glucose by the liver (American Diabetes Association, n.d.-a).

Sulfonylureas

Sulfonylureas are a group of diabetes drugs that bind to potassium channels on β cells and stimulate them to produce more insulin. They are effective in clients with diabetes who have functioning β cells. They are not effective in all clients with type 2 diabetes. Sulfonylureas may lose their effectiveness over time, requiring an increase in dosage (Costello et al., 2022).

SAFETY ALERT

Sulfonylureas

Sulfonylureas should be used cautiously with beta blockers. Beta blockers can mask the early symptoms of hypoglycemia, such as tachycardia and tremors. Also, when taken with a sulfonylurea, a nonselective beta blocker can prevent the body from compensating for hypoglycemia, resulting in critically low levels especially when the client is sleeping (Costello et al., 2022; Dimakos et al., 2023).

First-Generation Short-Acting Sulfonylureas

First-generation short-acting sulfonylureas lower blood glucose levels by causing the pancreas to produce insulin. These drugs were previously used along with diet, exercise, and, at times, other diabetes drugs to control type 2 diabetes; however, they have been discontinued for use in the United States with the development of second-generation sulfonylureas (Costello et al., 2022).

Second-Generation Sulfonylureas

Second-generation sulfonylureas increase insulin secretion through the pancreatic β cells. They are used along with diet, exercise, and sometimes other diabetes drugs to control glucose levels. Second-generation sulfonylureas typically have lower dosing, a longer duration of action, and fewer side effects than first-generation sulfonylureas. These drugs are metabolized in the liver and excreted in the urine. They should be used cautiously in clients with hepatic and renal impairment. Dosage usually begins with a low dose and is increased based on the client's glucose control needs (Costello et al., 2022).

Glipizide

Glipizide is a second-generation sulfonylurea that stimulates the pancreas to produce insulin, thereby lowering blood glucose levels. Glipizide is used along with diet and exercise to improve glucose homeostasis in adults with type 2 diabetes. Glipizide comes in tablet form and should be taken 30 minutes before the first meal of the day. It also comes in an extended-release form. The extended-release form should not be chewed, crushed, or broken and should be swallowed whole. The extended-release form should be taken with the first meal of the day.

Adverse effects of glipizide include headache, irritability, sweating, tachycardia, dizziness, nausea, blurred vision, feeling shaky, hypoglycemia, drowsiness, tremor, insomnia, myalgia, weight gain, and paresthesia. Serious adverse effects include agranulocytosis, aplastic anemia, thrombocytopenia, hepatic failure, and syndrome of inappropriate antidiuretic hormone (SIADH). Liver enzymes should be monitored closely when using this drug (National Library of Medicine, 2022b).

Glyburide

Glyburide is a second-generation sulfonylurea that stimulates the pancreas to produce insulin. Glyburide is used along with diet and exercise to control glucose levels. It comes in tablet form and is taken once or twice daily. Adverse effects include indigestion, flatulence, arthralgia (joint pain), blurred vision, dizziness, hypoglycemia, and irritability. This medication should be used cautiously with beta blockers because severe hypoglycemia may occur when they are taken together (National Library of Medicine, 2022c).

Glimepiride

Glimepiride, like glyburide and glipizide, is a second-generation sulfonylurea used along with diet and exercise to control blood glucose levels in the body. It is often used along with insulin to treat type 2 diabetes. Glimepiride comes in tablet form and is taken once daily with the first meal of the day. Adverse effects include dizziness, nausea, jaundice, upper abdominal pain, diarrhea, hypoglycemia, blurred vision, weight gain, and elevated serum alanine aminotransferase (ALT) levels (National Library of Medicine, 2022a; DailyMed, *Glimepiride*, 2021).

Non-Sulfonylurea Biguanides

Non-sulfonylurea biguanides are a group of oral diabetes drugs that prevent the production of glucose in the liver. They improve the body's sensitivity to insulin and reduce the amount of glucose absorbed by the intestines. Non-sulfonylurea biguanides are used to treat type 2 diabetes (Corcoran & Jacobs, 2022).

Metformin is a non-sulfonylurea biguanide. It is used to treat type 2 diabetes along with diet, exercise, and sometimes other diabetes drugs or insulin. Metformin comes as an immediate release tablet, an extended-release tablet, and an oral solution. Adverse effects include dizziness, headache, weakness, hypoglycemia, palpitations, flushing, nausea, vomiting, diarrhea, and flatulence. Metformin should be used cautiously in older clients and in clients with renal and hepatic impairments. Clients should not drink alcohol while taking metformin (Corcoran & Jacobs, 2022).

! SAFETY ALERT

Metformin and Contrast Dye

Contrast dye can increase the risk of lactic acidosis (when lactic acid production exceeds lactic acid clearance in the body) in clients who are taking metformin and have decreased renal function. Metformin should be withheld 24 hours prior to and for 48 hours after contrast dye administration if the estimated glomerular filtration rate (eGFR) is less than 30 mL/min (Yale School of Medicine, 2022).

FDA BLACK BOX WARNING

Metformin

Lactic acidosis is a rare but potentially severe consequence of therapy with the non-sulfonylurea biguanide metformin.

Alpha-Glucosidase Inhibitors

Alpha-glucosidase inhibitors lower blood glucose levels by inhibiting enzymes such as amylase, maltase, and sucrose in the GI tract, thus delaying the digestion and intestinal absorption of carbohydrates (Akmal & Wadhwa, 2022).

Acarbose

Acarbose was the prototype alpha-glucosidase inhibitor. It delays digestion and absorption of carbohydrates to diminish the increase in blood glucose levels after meals. Acarbose is rapid acting and peaks in 1 hour. It is metabolized by the GI tract and excreted in the urine and feces. Adverse effects include nausea, vomiting, diarrhea, malabsorption, leukopenia, thrombocytopenia, and anemia. It is contraindicated for use in clients with severe renal and hepatic impairments (Feingold, 2022).

Miglitol

Miglitol slows the digestion of carbohydrates. It is used in combination with diet, exercise, and sometimes other drugs to control blood glucose levels. It is rapidly absorbed and excreted in the urine. Adverse effects include bloating, flatulence, diarrhea, and abdominal pain or cramping (Feingold, 2022).

Thiazolidinediones

Thiazolidinediones lower blood glucose levels by decreasing insulin resistance. They are referred to as “glitazones” or “insulin sensitizers” (Feingold, 2022; Eggleton & Jialal, 2023).

Pioglitazone hydrochloride is a thiazolidinedione that is used along with diet and exercise to decrease blood glucose levels. It works to enhance the body’s response to insulin, thereby decreasing glucose in the blood. Adverse effects include muscle pain, weight gain, sore throat, blurred vision, and tooth problems. Pioglitazone hydrochloride is contraindicated in those with liver impairment (Feingold, 2022).

Meglitinides

Meglitinides lower blood glucose levels by stimulating the pancreas to secrete insulin. This class of drug has the potential to produce rapid, short-lived insulin output in those with type 2 diabetes. Because of the rapid onset and short duration of action with these drugs, they should be administered 1–30 minutes prior to meals (Feingold, 2022).

Repaglinide is a meglitinide that works in clients with type 2 diabetes by closing potassium channels in the pancreatic beta cells, thereby increasing insulin secretion, which lowers glucose levels in the blood. It is absorbed through the GI tract and peaks in 1–1.5 hours. Metabolism occurs in the liver, and it is excreted in the urine and feces. Adverse effects include GI upset, upper respiratory infections, and hypoglycemia. It is contraindicated for use in those with type 1 diabetes and those with diabetic ketoacidosis (Feingold, 2022).

Dipeptidyl Peptidase 4 (DDP 4) Inhibitors

Dipeptidyl peptidase 4 inhibitors block the action of dipeptidyl peptidase 4, an enzyme that destroys incretin. Incretin helps the body produce insulin only when it is needed to reduce the excess amount of glucose being produced by the liver. DDP 4 inhibitors are used to treat type 2 diabetes (Kasina & Baradhi, 2022).

Sitagliptin

Sitagliptin is a DDP 4 inhibitor used to treat type 2 diabetes. It is rapidly absorbed, peaks in 1–4 hours, and has a 12-hour half-life. It is mainly excreted through the urine. Adverse effects include runny nose, sore throat, headache, and upper respiratory infections. Hypoglycemia may occur when used in combination with other drugs. Sitagliptin is

contraindicated in those with congestive heart failure (Zhou et al., 2019).

Linagliptin

Linagliptin, like sitagliptin, is a DDP 4 inhibitor used to treat type 2 diabetes. It is rapidly absorbed and long acting. It peaks in 1.5 hours and has a 12-hour half-life. Adverse effects include bloating, skin rash, stomach pain, back pain, and joint pain. It should be used cautiously in those with hypersensitivity, exfoliative dermatitis, or bronchial hypersensitivity (Gharabaghi et al., 2022).

Selective Sodium Glucose Transporter 2 (SGLT2)

Selective sodium glucose transporter 2 drugs are used to treat clients with type 2 diabetes. SGLT2 drugs lower blood glucose levels by blocking the reabsorption of glucose in the kidneys and promoting the excretion of glucose in the urine (Padda et al., 2022).

Dapagliflozin

Dapagliflozin is an SGLT2 drug that reduces reabsorption of filtered glucose and thereby promotes urinary glucose excretion. It is rapidly absorbed and peaks in 2 hours. It is metabolized in the liver and excreted mainly in the urine. Adverse effects include increased urination, skin rash, dehydration, hypotension, back pain, and genital infections including UTIs. It is contraindicated in those with renal impairment (Dhillon, 2019).

Empagliflozin

Empagliflozin is an SGLT2 drug that is rapidly absorbed. It peaks in 1.5 hours. Empagliflozin is metabolized by the liver and excreted mainly in the urine. Adverse effects include increased urination, bladder pain, painful urination, vaginal irritation or discharge, and pain during intercourse. It is contraindicated in those with renal impairment (Sizar et al., 2022).

Fixed Combination Oral Diabetes Drugs

Fixed combination oral diabetes drug therapy may be required in the control of type 2 diabetes. Combination oral diabetes drug therapy is used when monotherapy, diet, and exercise alone cannot control blood glucose levels. Although in the past these drugs were taken as separate tablets, several fixed-dose single-tablet combinations have been manufactured (Kalra et al., 2020).

LINK TO LEARNING

New in Oral Diabetes Medicines: Non-Insulin Injectables

Access multimedia content (https://openstax.org/books/pharmacology/pages/28-3-oral-antidiabetic-drugs)
In this video, Lisa Kroon, a Doctor of Pharmacy, describes general treatments for glycemic control (hyperglycemia) in people with type 2 diabetes.

Glyburide-Metformin

Glyburide-metformin is a combination of a second-generation sulfonylurea and a non-sulfonylurea biguanide. It is used in conjunction with diet and exercise for clients with type 2 diabetes that was not controlled with a monotherapy diabetes drug. Dosing is a combined tablet of 1.25 mg glyburide and 250 mg metformin one to two times daily. The maximum dose is 20 mg glyburide and 2000 mg metformin daily. It is not recommended for use in children. Adverse effects include blurred vision, drowsiness, excessive hunger, headache, nausea, nervousness, sore throat, and unusual tiredness. Glyburide-metformin is contraindicated in those with severe renal and liver impairment. Those with congestive heart failure should use it cautiously because this drug may increase the risk of myocardial infarction (Shuster et al., 2020).

Sitagliptin-Metformin

Sitagliptin-metformin is a fixed-dose combination diabetes drug that combines a dipeptidyl peptidase 4 inhibitor and a non-sulfonylurea biguanide. Sitagliptin-metformin is used to treat type 2 diabetes when the diet, exercise, and monotherapy diabetes drugs were ineffective. The recommended starting dose in clients not currently treated with metformin is 50 mg sitagliptin and 500 mg metformin HCl twice daily, with gradual dose escalation recommended to reduce gastrointestinal side effects associated with metformin. The starting dose in clients already treated with

metformin should provide sitagliptin dosed as 50 mg twice daily (100 mg total daily dose) and the dose of metformin already being taken. For clients taking metformin HCl 850 mg twice daily, the recommended starting dose of sitagliptin-metformin is 50 mg sitagliptin and 1000 mg metformin HCl twice daily. The maximum recommended daily dose is 100 mg of sitagliptin and 2000 mg of metformin hydrochloride (HCl). Adverse effects include diarrhea, upper respiratory tract infection, headache, nausea, vomiting, abdominal pain, hypoglycemia, EKG changes, pancreatitis, acute renal failure, myalgia, and pain in extremity (DailyMed, *Sitagliptin,* 2023; He et al., 2021).

Liraglutide-Insulin Degludec

Liraglutide-insulin degludec is a fixed-dose combination of liraglutide and insulin degludec. It is used to treat type 2 diabetes when diet, exercise, and drug monotherapy were ineffective. It comes in a subcutaneous pen similar to an insulin pen. The pen is a combined dose of insulin degludec 50 units and liraglutide 1.8 mg. Adult and pediatric dosing is based on the client's blood glucose level and must be determined by the health care provider. Adverse effects include bloating, blurred vision, chills, confusion, constipation, dry mouth, headache, hives, increased hunger, lightheadedness, muscle aches, nausea, sweating, tachycardia, and trouble swallowing. It is contraindicated in those with hypoglycemia, pancreatitis, and hypersensitivity (DailyMed *Victoza, Liraglutide injection*, 2023).

UNFOLDING CASE STUDY

Part B

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up to Case Study Part A.

Alaina Sanders was diagnosed with type 2 diabetes, and the health care provider prescribed extended-release glipizide 5 mg orally and lifestyle modifications. The client returns to her health care provider's office today for a 6-month follow-up appointment after starting drug treatment and lifestyle modifications.

Laboratory Results
Glycosylated hemoglobin

6 Months Ago
7.8%

Today
6.9%

Vital Signs		Physical Examination
Temperature:	97.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention or peripheral edema. S1, S2 heard on auscultation. • *Respiratory:* Breath sounds clear bilaterally • *GI:* Abdomen soft, nontender, nondistended • *GU:* Within normal limits • *Neurological:* Within normal • *Integumentary:* No wounds noted; skin appropriate for age
Blood pressure:	108/72 mm Hg	
Heart rate:	84 beats/min	
Respiratory rate:	18 breaths/min	
Oxygen saturation:	97% on room air	
Height:	5'5"	
Weight:	173 lb	

TABLE 28.6

3. Which statement by the client indicates to the nurse that Alina understands her treatment plan?

a. "I take extended-release glipizide with my breakfast."
b. "I take extended-release glipizide with dinner."
c. "I chew my extended-release glipizide tablet."
d. "I should watch for hyperglycemia while taking extended-release glipizide."

4. Based on the client's glycosylated hemoglobin results, which treatment plan does the nurse anticipate the health care provider will prescribe?
a. No changes to the treatment plan
b. Increase glipizide to 10 mg daily
c. Change to another oral diabetic drug
d. Add insulin lispro 6 units daily

Hypoglycemia Drugs

Hypoglycemia drugs raise blood glucose levels. These drugs are used to treat severe hypoglycemia and hypoglycemic reactions that are often associated with diabetes. They are used after conservative measures to treat severe hypoglycemia are ineffective (Mathew & Thoppil, 2022).

Glucagon

Glucagon is a hormone secreted by alpha (α) cells of the islets of Langerhans in the pancreas. Glucagon increases blood glucose levels by stimulating glycogen breakdown in the liver. Peak time is 15 minutes after dosing. Glucagon comes as an injectable and as a nasal spray. Adult and pediatric dosing is based on the client's age and weight. Glucagon is used when the client is semiconscious, unconscious, or unable to ingest sugar-containing food. Blood glucose levels should be reassessed 15 minutes after administering this drug. Adverse effects include nausea, vomiting, and temporary tachycardia. Glucagon is contraindicated in clients with hypersensitivity and with known **pheochromocytoma** (Morris & Baker, 2022).

Diazoxide

Diazoxide is a non-diuretic benzothiadiazine and works by inhibiting insulin release from the pancreas by opening potassium channels in the beta cell membrane. It is used to treat hypoglycemia in clients with hyperinsulinemia. This drug is also a vasodilator and used to treat hypertensive emergencies. It is rapidly absorbed and highly protein bound. Diazoxide is metabolized by the liver and mainly excreted by the kidneys. The usual adult daily oral dosage is 3–8 mg/kg, divided into two or three equal doses every 8 or 12 hours. Its onset is 1 hour, and its duration is 8 hours. Adverse effects include anorexia, nausea, vomiting, abdominal pain, tachycardia, palpitations, and increased uric acid levels. Diazoxide is contraindicated in clients with a hypersensitivity to sulfonamide and thiazide diuretics (Chen et al., 2021).

Table 28.7 lists common oral diabetes drugs and typical routes and dosing for adult clients (with pediatric exception note for metformin).

Drug	Routes and Dosage Ranges
Acarbose (Precose)	25 mg orally 3 times daily with meals. Maximum dose: 300 mg daily.
Dapagliflozin (Farxiga)	Dosage is adjusted based on estimated glomerular filtration rate (eGFR): • *eGFR ≥45:* 5–10 mg orally once daily. • *eGFR 25 to ≤45:* 10 mg orally once daily. • *eGFR less than 25:* Not recommended.
Empagliflozin (Jardiance)	10 mg orally once daily. Maximum dose: 25 mg daily. Data are insufficient to provide a dosage recommendation in clients who have type 2 diabetes mellitus and established cardiovascular disease with an eGFR <30 mL/min/1.73 m^2 or heart failure with an eGFR <20 mL/min/1.73 m^2.

TABLE 28.7 **Drug Emphasis Table: Oral Diabetes Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Glipizide (Glucotrol, Glucotrol XL)	5 mg orally daily 30 minutes before breakfast. Maximum dose: 40 mg daily. *Extended release:* Once daily with breakfast.
Glyburide/ metformin (Glucovance)	1.25 mg glyburide/250 mg metformin orally daily. Titrate 2 weeks after initial dosing up to 1.25 mg glyburide/250 mg metformin orally every 12 hours. Maximum dose: 20 mg glyburide/2000 mg metformin orally daily.
Liraglutide/ insulin degludec (Xultrophy)	10 units insulin degludec/3.6 mg of liraglutide subcutaneously once daily. Maximum dose: 50 units insulin degludec/1.8 mg liraglutide subcutaneously daily.
Metformin (Glucophage, Glucophage XR)	*Immediate release:* *Adults:* 500–1000 mg orally twice daily. Maximum dose: 2000 mg daily. *Children (the only oral diabetes drug that is safe for use in children 10–17 years of age):* 500 mg orally twice daily. Maximum dose: 2000 mg daily in divided doses. *Extended release:* *Adults:* 250–500 mg once daily with evening meal; increase dose by 500 mg/week on the basis of glycemic control and tolerability. Maximum dose: 2000 mg/day. *Children:* Health care provider should determine dose based on body surface area and glucose target range. *Oral solution:* *Adults and children:* 500 mg/5 mL daily up to a maximum dose of 2000 mg/day.
Miglitol (Glyset)	25 mg orally 3 times daily at the start of each meal. Maximum dose: 200 mg 3 times daily.
Pioglitazone (Actos)	15–30 mg orally once daily. Maximum dose: 45 mg daily.
Repaglinide (Prandin)	0.5–4 mg orally 3–4 times daily, 15–30 minutes before meals. Maximum dose: 16 mg daily.
Sitagliptin (Januvia)	100 mg orally daily. *For clients with an eGFR ≥45 mL/min/1.73 m^2 to <90 mL/min/1.73 m^2:* No dosage adjustment required. *For clients with moderate renal impairment (eGFR ≥30 mL/min/1.73 m^2 to <45 mL/min/1.73 m^2):* 50 mg once daily. *For clients with severe renal impairment (eGFR <30 mL/min/1.73 m^2) or with end-stage renal disease (ESRD) requiring hemodialysis or peritoneal dialysis:* 25 mg once daily. May be administered without regard to the timing of dialysis.
Sitagliptin/ metformin (Janumet)	*Clients not currently treated with metformin:* Initial dose: 50 mg sitagliptin/500 mg metformin orally twice daily with gradual escalation. *Clients already treated with metformin:* Initial dose: 50 mg sitagliptin twice daily and the dose of metformin already being taken. Maximum dose: 100 mg sitagliptin/2000 mg metformin orally daily.

TABLE 28.7 **Drug Emphasis Table: Oral Diabetes Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects of oral diabetes drugs include gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal discomfort), hypoglycemia (symptoms include dizziness, shakiness, sweating/chills, clammy skin, feeling faint, agitation, confusion, blurred or impaired vision), fluid retention, weight gain, and headache.

Contraindications include hypersensitivity to the drug or any of its components, severe kidney disorders (as most of these drugs are excreted in the urine and can further impair renal function), hepatic insufficiency (as most of these drugs are metabolized by the liver and can result in further impaired hepatic function), and disorders with fluid retention (such as heart failure and renal failure, as these drugs can cause additional fluid retention and volume overload).

Table 28.8 is a drug prototype table for oral diabetes drugs featuring metformin. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Non-sulfonylurea biguanide **Mechanism of Action** Decreases intestinal absorption of glucose and improves insulin sensitivity by increasing glucose uptake	**Drug Dosage** *Immediate release:* *Adults:* 500–1000 mg orally twice daily. Maximum dose: 2000 mg daily. *Children (the only oral diabetes drug that is safe for use in children 10–17 years of age):* 500 mg orally twice daily. Maximum dose: 2,000 mg daily in divided doses. *Extended release:* *Adults:* 250–500 mg once daily with evening meal; increase dose by 500 mg/week on the basis of glycemic control and tolerability. Maximum dose: 2000 mg/day. *Children:* Health care provider should determine dose based on body surface area and glucose target range. *Oral solution:* *Adults and children:* 500 mg/5 mL daily up to a maximum dose of 2000 mg/day.
Indications To control hyperglycemia in those with type 2 diabetes **Therapeutic Effects** Decreases glucose production in the liver by reducing gluconeogenesis Reduces glucose absorption from the intestines	**Drug Interactions** Alcohol Dolutegravir Ginseng Psyllium Contrast dye **Food Interactions** Fiber-rich foods Grapefruit juice Guar gum
Adverse Effects Dizziness/weakness Headache Hypoglycemia Palpitations Flushing Nausea/vomiting/diarrhea/flatulence Abdominal pain Weight loss Vitamin B_{12} deficiency	**Contraindications** Renal and hepatic impairment Metabolic acidosis Megaloblastic anemia History of myocardial infarction Caution: Monitor closely for signs of hypoglycemic reaction; use cautiously in older clients with renal and hepatic impairments

TABLE 28.8 **Drug Prototype Table: Metformin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking oral diabetes drugs:

- Assess the client's knowledge about diabetes, signs and symptoms, and treatment and clarify any gaps in knowledge.
- Monitor blood glucose levels as ordered and as needed when symptoms of hypoglycemia/hyperglycemia are present.
- Provide client teaching regarding how the drug is administered and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an oral diabetes drug should:

- Report symptoms of hypoglycemia such as headache, nervousness, sweating, clammy skin, tremor, and tachycardia.
- Report symptoms of hyperglycemia such as increased thirst, increased urine output, hot/dry skin, sweet, fruity breath odor, and ketones in urine.
- Keep 15 grams of carbohydrates on hand in case of a hypoglycemic reaction. Orange juice, graham crackers, and hard candy are appropriate carbohydrate choices during hypoglycemia.
- Show family members and their support system how to administer glucagon during a hypoglycemic reaction if the client cannot eat or drink or is unconscious.
- Keep a blood glucose journal for tracking blood glucose levels.
- Make lifestyle modifications as directed by their health care provider, such as diet, exercise, and weight loss, to help control blood glucose levels.

The client taking an oral diabetes drug *should not:*

- Drink alcohol with oral diabetes agents because it may impair hepatic function.

Chapter Summary

This chapter focused on managing diabetes with the use of drugs and insulin products. Type 1, type 2, and gestational diabetes were defined, along with the importance of recognizing the difference between hypoglycemia and hyperglycemia. Specific diagnostic tests for diabetes were described. Disease prevention was briefly discussed.

Common diabetic drugs were covered in this chapter. Insulin was defined, and types of insulin were discussed. Insulin administration sites were also presented. Additional drug classifications covered included non-insulin injectable drugs, oral drugs, and drugs to treat hypoglycemic reactions.

Key Terms

basal insulin dosing an important component in diabetes management because it acts as a background insulin that is designed to stabilize blood glucose levels during times of fasting

bolus a single dose of a drug being administered

continuous glucose monitor a device that monitors blood glucose levels on a continual basis

diabetes a disease that results from a deficiency in insulin that leads to alterations in the metabolism of glucose, fats, and proteins

fasting blood glucose a test that measures the blood sugar level after an overnight fasting period

glycosylated hemoglobin (A1c) a test that measures the blood sugar level over the past 60 to 90 days

hyperglycemia a condition that occurs when the blood glucose level in the body is above the normal range of 70–110 mg/dL and the body has too little insulin or is insulin resistant, making it unable to lower the blood glucose level on its own

hypoglycemia a condition that occurs when the blood glucose level in the body falls below the normal range of 70–110 mg/dL

insulin a hormone released by β cells from the islets of Langerhans in the pancreas after eating a meal that helps the body's cells absorb glucose for energy

insulin pen a pen-shaped injector device that combines insulin and a syringe in one unit; insulin pens are prefilled with an insulin cartridge or have a prefilled insulin reservoir

insulin pump a small, computerized infusion set device that delivers insulin

ketoacidosis a life-threatening condition that occurs when the body breaks down fat too quickly, causing the liver to produce ketones, which in turn causes the blood to become acidic

non-insulin injectable diabetes drugs drugs that provide an alternative to insulin therapy for those with type 2 diabetes; they act on hormones that are secreted along with insulin by the pancreas to control glucose homeostasis

oral diabetes drugs drugs used to treat type 2 diabetes by lowering blood glucose levels

peak time the time during which insulin is at its maximum strength in terms of lowering blood glucose levels; individuals are at a higher risk of developing hypoglycemic symptoms when insulin is peaking

pheochromocytoma a rare non-cancerous tumor that develops in the adrenal gland that causes an excessive release of adrenal hormones

polydipsia increased thirst

polyphagia increased hunger

polyuria frequent urination

random blood glucose a test that measures the blood sugar level at the time tested

sliding scale coverage varying the dose of insulin based on the blood glucose level

subcutaneous situated or applied under the skin

titrated continuously measuring and adjusting the balance of a drug dosage

type 1 diabetes an autoimmune disorder in which the body's immune system attacks and destroys the β cells in the pancreas that make insulin, resulting in elevated blood glucose levels

type 2 diabetes a disorder that occurs as a result of the body not making enough insulin or not using insulin well

Review Questions

1. A nurse is assessing a client for type 1 diabetes. Which of the following findings should the nurse expect if the client does, in fact, have diabetes?
   a. Hemoglobin A1c 5.6%
   b. Fasting blood glucose 101 mg/dL
   c. Random blood glucose 150 mg/dL
   d. Glycosylated hemoglobin 6.8%

2. A nurse is developing an education plan for a client with diabetes in regard to an insulin pump. Which of the following should the nurse include in the education plan?
   a. Teach the client to rotate sites for insulin injections
   b. Teach the client to recognize symptoms of hypoglycemia
   c. Teach the client how to administer insulin injections
   d. Teach the client how to obtain a glycosylated hemoglobin once a month

3. A nurse is administering regular insulin to a client with diabetes. After administering the correct dose at 6:30 a.m., the nurse should ensure the client receives breakfast at which of the following times?
   a. 7 a.m.
   b. 8 a.m.
   c. 9 a.m.
   d. 10 a.m.

4. A nurse is caring for a client with type 1 diabetes who is being prescribed a long-acting insulin. The nurse identifies which of the following as a long-acting insulin?
   a. Insulin lispro
   b. Insulin glargine
   c. Human regular insulin
   d. Insulin isophane NPH

5. A nurse is teaching a client with diabetes about a new prescription for insulin isophane NPH. Which of the following instructions should the nurse include in the teaching?
   a. Discard the insulin isophane NPH if cloudy.
   b. Take insulin isophane NPH 15 minutes before meals.
   c. Eat a snack 7 hours after taking the insulin isophane NPH.
   d. Rotate insulin isophane NPH injection sites once a week.

6. A nurse is caring for a client with diabetes who has a blood glucose of 50 mg/dL and is semiconscious and having difficulty swallowing. Which of the following actions should the nurse take?
   a. Administer a routine dose of glyburide
   b. Administer 15 grams of carbohydrates
   c. Give the client a glass of orange juice
   d. Administer glucagon

7. A nurse is preparing to administer 15 units of regular insulin and 23 units of NPH insulin subcutaneously. What is the total number of units of insulin that the nurse should prepare in the insulin syringe?
   a. 15 units
   b. 23 units
   c. 38 units
   d. 12 units

8. Which of the following insulins can be administered via an insulin pump?
   a. Insulin glargine
   b. Insulin isophane NPH
   c. Insulin aspart
   d. Insulin detemir

9. A 76-year-old client with diabetes and renal impairment is scheduled for a diagnostic test requiring the use of contrast dye. Which of the following drugs should the nurse instruct the client to stop taking 24 hours prior to the procedure?
   a. Metformin
   b. Insulin lispro

c. Glipizide
d. Linagliptin

10. A nurse received a health care provider's order to administer 750 mg of metformin twice daily to a client. Metformin is available in 500 mg tablets. How many tablets will the nurse administer per dose?
a. 1.5 tablets
b. 2 tablets
c. 3 tablets
d. 4 tablets

CHAPTER 29
Introduction to the Digestive System

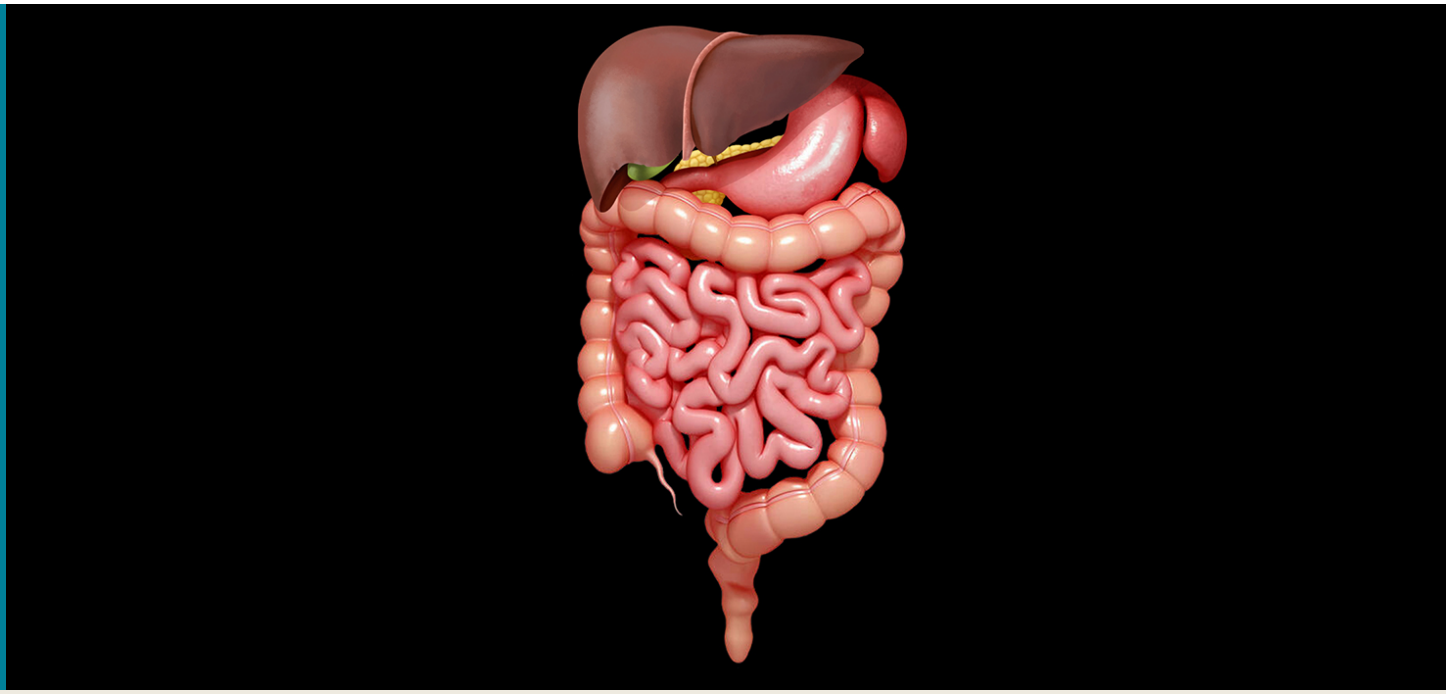


FIGURE 29.1 The digestive system breaks down food into nutrients that can be absorbed into the bloodstream to give the body energy and the ability to grow and repair itself. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The digestive system is continuously at work, yet people seldom appreciate the complex tasks it executes in a choreographed biologic performance. Eating may be one of the simple pleasures in life, but digesting even one apple requires the coordinated work of many organs. This chapter will introduce the digestive system and some common conditions that can alter any one of its functions.

29.1 Introduction to the Gastrointestinal System and Oral Cavity

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 29.1.1 Describe the structure and function of the gastrointestinal system and oral cavity.
- 29.1.2 Discuss common conditions that affect the gastrointestinal system and oral cavity.

Gastrointestinal System

The digestive system consists of the gastrointestinal (GI) tract and accessory organs. The GI tract is also known as the **alimentary canal**. Together with the accessory organs, the GI tract provides nutrition and hydration to the body through the processes of **ingestion**, **digestion**, **absorption**, and **metabolism**. A healthy GI system with functional digestive processes is essential to break down and absorb nutrients from food and liquids to provide energy and growth to the human body. The ability to assimilate nutrients and hydration is crucial to cellular maintenance and repair. The final phase of digestion is to eliminate waste material not used by the body.

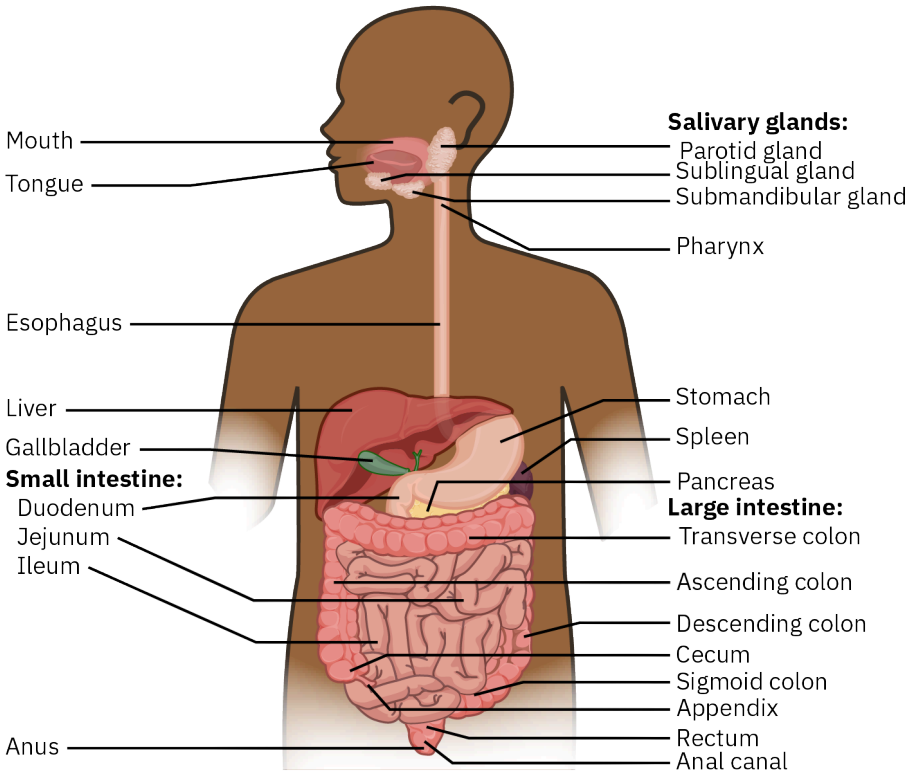


FIGURE 29.2 All digestive organs play integral roles in the life-sustaining process of digestion. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The GI tract and accessory organs form one continuous structure from the mouth to the anus (Figure 29.2). Ingestion is the process of taking in food, generally by the mouth. Digestion is a systematic process that breaks down food into its simplest form to promote absorption and moves this food and fluids through the GI tract. The complex digestive process starts with the **mastication** process as a person uses their teeth to bite and chew food. This is referred to as the mechanical phase of digestion. In the mouth, the food mixes with **saliva** from the salivary glands. Muscles in the pharynx allow the mixed food to be swallowed as a bolus. The bolus continues to travel through the GI tract, passing through the esophagus into the stomach. The stomach is the basic organ of digestion. The stomach further mixes the bolus and blends it with acidic gastric juices and **pepsin** to digest protein. This process produces **chyme**. At this point, the liver, pancreas, and gallbladder further aid the digestive process by adding **bile** and bicarbonate before the chyme is released into the small intestine. These substances help protect the small intestine from being destroyed by the acidic chyme. The digestive enzymes and **hydrochloric (HCl) acid** are part of the chemical phase of digestion, which continues as the food travels to the small intestine. Nutrients are absorbed into the blood or lymph in the small intestine. Water, along with some vitamins and minerals, is absorbed in the large intestine. Material not assimilated and absorbed results in waste products that leave the body through the anus. Table 29.1 provides an overview of the organs of the GI system and their functions.

Major Organs of the GI System	Function
Mouth/oral cavity	When food enters the mouth for nourishment, processes of sensory stimulation, mechanical processing, and lubrication begin. The salivary glands secrete amylase and ptyalin to begin to break down starches. Lipase is secreted by the salivary glands to break down fats.
Pharynx	Commonly called the throat, the pharynx is a passageway for food to the esophagus.

TABLE 29.1 Gastrointestinal System Organs

Major Organs of the GI System	Function
Esophagus	The esophagus empties food materials into the stomach through peristalsis during swallowing. It secretes large amounts of mucus, which helps lubricate food.
Stomach	The upper muscles relax to let food and fluids enter the stomach; the lower muscles churn and mix food with digestive juices to form chyme and start the breakdown of proteins. Minimal absorption of nutrients occurs in the stomach; rather, it secretes proteases such as pepsin (breaks down protein into amino acids), amylase (breaks down carbohydrates into sugars), and lipase (breaks down fats into glycerol and fatty acids).
Small intestine (duodenum, jejunum, ileum)	The small intestine is responsible for the absorption of 90%–95% of food with the aid of the pancreatic enzymes (amylase, trypsin, and lipase) and enzymes secreted in the intestine (maltase, sucrase, lactase, and peptidase).
Large intestine	The large intestine receives unabsorbed and undigested food material (waste products), absorbs water and electrolytes, and forms feces.
Anus	The anus is responsible for defecation.
Accessory Organs of the GI System	**Function**
Teeth	The teeth bite and chew (masticate) food as the first step in digestion.
Tongue	The tongue is a muscular organ that helps with mastication and assists in swallowing the food bolus.
Salivary glands	Located in the mouth are three pairs of salivary glands (parotid, sublingual, submandibular) that secrete saliva (consisting of water, amylase, lipase, electrolytes, mucus, immunoglobins, and amino acids) and digestive enzymes. The main role of saliva is to lubricate the mouth, moisten the food bolus, and start the digestive process.
Pancreas	The pancreas produces enzymes to digest proteins (trypsin and chymotrypsin), carbohydrates (amylase), and fats (lipase).
Liver	The liver makes and secretes bile (which includes cholesterol, bile acids, and bilirubin). Bile helps emulsify fats into fatty acids, aiding lipid absorption.
Gallbladder	The gallbladder stores and concentrates bile.

TABLE 29.1 **Gastrointestinal System Organs**

The average length of the adult human GI tract is about 30 feet from the mouth to the anus. Under normal conditions, nutrients are introduced into the human body through the mouth as food and fluids. As food and fluids move through the GI tract, they are transformed into useful nutrients to be assimilated into the body's cells for survival and homeostasis. The breakdown and assimilation depend on the large surface area of the GI tract, which has traditionally been described as the size of a tennis court. However, recent literature notes that the surface area is much smaller. According to Rao and Johncy (2022), using geometric comparisons to approximate the intestinal surface area is inappropriate.

Multiple factors play a role in GI functions and health. Structural and nutritional deficiencies can alter the function of tissues and organs. Intestinal transit time, or how quickly food and fluids move through the GI tract, may also impact GI functions and health. Intestinal transit time varies based on age. Transit time is slower in newborns and gradually increases, starting at about 4 months of age. The transit time slows again in older adults due to an aging GI system with decreased GI **peristalsis** (muscular contractions and relaxations that propel food through the GI tract), motility, and intestinal blood flow. The aging GI system, coupled with medications that may alter absorption of food and fluids, can cause the most common GI complaints: constipation and diarrhea. Although these are some of the most frequent GI concerns in older adults, these uncomfortable conditions can affect people of any age.

Oral Cavity

The oral cavity is the beginning of the digestive tract (Figure 29.3). The oral cavity refers to the structures of the mouth: the upper and lower lips, teeth, gingiva (gums), hard and soft palate, uvula, retromolar trigone, tonsils, floor of the mouth, tongue, salivary glands, and buccal mucosa. The teeth are vital for breaking up food (mastication) for digestion and absorption. Mastication is the essential first step in digestion. The tongue is a strong muscle that facilitates mastication by mixing food and helping to form it into a bolus, which is the first step in swallowing. The tongue is also involved in the sensation of taste through taste buds. Taste buds are specialized cells that communicate the sense of taste (sweet, salty, sour, bitter, and umami) to the brain.

Salivary glands located in and around the mouth have many functions for oral health and digestion. The three types of salivary glands—sublingual, submandibular, and parotid—produce saliva to keep the oral cavity moist and lubricated to promote digestion and optimal oral health. In an adult, the salivary glands produce up to 2 L of saliva every day (Cleveland Clinic, n.d.). The presence of food increases saliva secretion. This is a parasympathetic response mediated by two cranial nerves, the facial nerve (cranial nerve VII) and the glossopharyngeal nerve (cranial nerve IX). Saliva helps protect the teeth from cavity-causing bacteria as well as maintain the pH balance in the mouth, but the most appreciated role of saliva is that of digestive aid. It helps moisten food to facilitate the swallowing of chewed food. Saliva contains an enzyme, amylase, to help break down foods, particularly complex carbohydrates (starches) into simple and more easily digested sugars. The enzymes in saliva kick-start the digestive process in addition to helping food travel through the esophagus to the stomach for further digestion.

Any disorder of the mouth or oral cavity may disrupt the digestive process. Common disorders such as “cold sores” from a herpes simplex virus (HSV), canker sores, mucositis, and candida infections may affect the oral cavity. These can be painful conditions. A thorough nursing history is essential to determine the source of any pain in order to alleviate it and ensure the client’s ability to eat. The nursing health history should include questions about oral health and dental practices, home-based treatments, and the use of both over-the-counter and prescription medications. A thorough physical examination of the oral cavity is equally important because careful inspection of the oral cavity may uncover issues that can impair biting and chewing. Nurses should teach clients that good oral hygiene is essential for this first step in digestion.

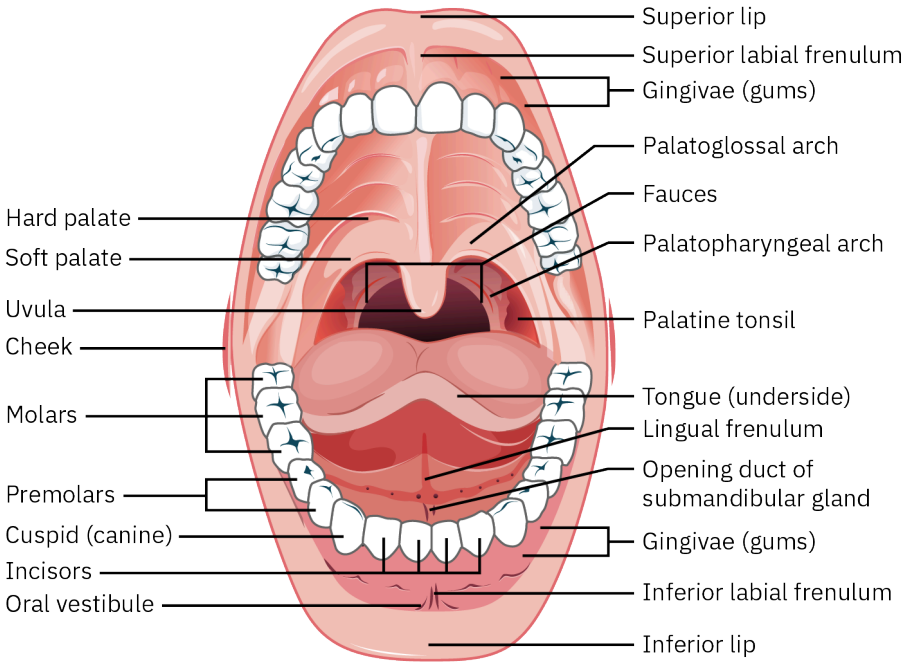


FIGURE 29.3 The mouth includes the lips, tongue, hard and soft palate, gums, and teeth. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

29.2 Introduction to the Esophagus and Stomach

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 29.2.1 Describe the structure and function of the esophagus and stomach.
- 29.2.2 Discuss common conditions that affect the esophagus and stomach.

Esophagus

The esophagus is a muscular tube at the base of the pharynx behind the trachea (Figure 29.4). The esophagus is approximately 10 inches long and extends to the stomach. Its primary function is to move food and fluids from the mouth to the stomach for digestion. The **upper esophageal sphincter** and the **lower esophageal sphincter** are two structures within the esophagus that control the movement of food and liquid. The sphincters are ringlike bands of smooth muscle fibers that function as valves to protect the body by propelling food and fluids through the esophagus and into the stomach. These neuromuscular sphincters open and close in response to autonomic nervous system stimulation and control.

The upper esophageal sphincter, also known as the oropharyngeal sphincter, is located between the pharynx and the mouth. A properly functioning upper esophageal sphincter is vital to prevent **aspiration** of food and liquids into the airways. Another structural membrane that prevents aspiration is the **epiglottis**. The epiglottis is a sheetlike flap that closes over the trachea to prevent food and fluids from entering the lungs (aspiration).

The lower esophageal sphincter is located where the esophagus meets the stomach. It is commonly referred to as the gastroesophageal sphincter because of its location between the esophagus and the stomach. It is also sometimes referred to as the cardiac sphincter because it is located close to the heart.

If either of the esophageal sphincters is not functioning properly, ingested food, fluids, and acidic stomach contents may move backward into the esophagus, causing irritation or damage to the tissues. Common problems with the esophagus include GI inflammation, esophagitis, **gastroesophageal reflux disease (GERD)**, esophageal varices, and hiatal hernia. Structural defects in the esophagus may also cause problems such as obstruction. Esophageal dysfunction often interferes with nutrition and at times may cause varying degrees of discomfort. Medications are often used to alleviate uncomfortable symptoms and prevent further symptoms and potential complications.

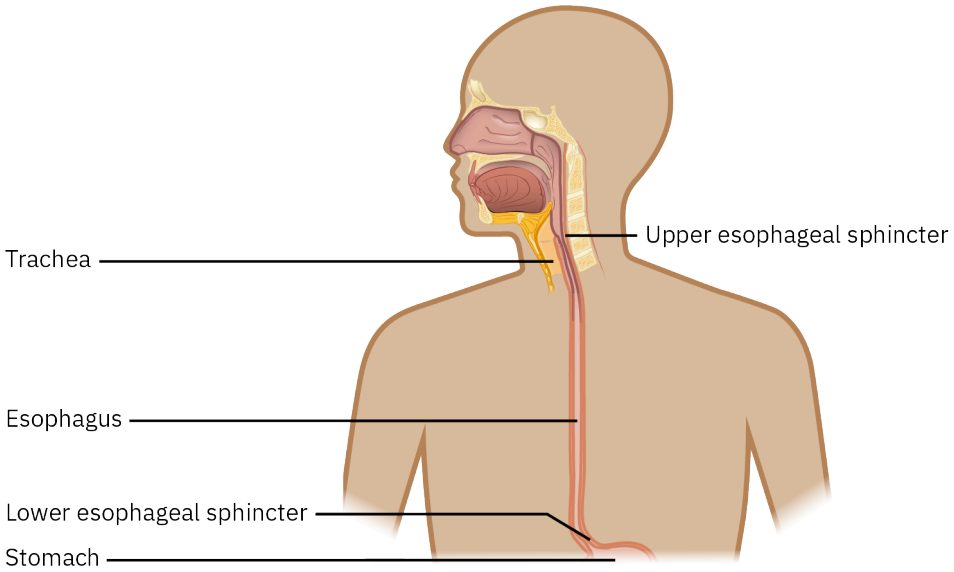


FIGURE 29.4 The upper esophageal sphincter controls the movement of food from the pharynx to the esophagus. The lower esophageal sphincter controls the movement of food from the esophagus to the stomach. (credit: modification of work from *Anatomy and Physiology 2e.* attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Stomach

The stomach plays an essential role in mechanical and chemical digestion yet is dependent on many different body structures, functions, and processes (Figure 29.5). Located in the upper part of the abdomen, the stomach has four parts: the cardia (the opening from the esophagus into the stomach), the fundus (the expanded upper portion), the body (the central and largest portion), and the pylorus (the lowest portion).

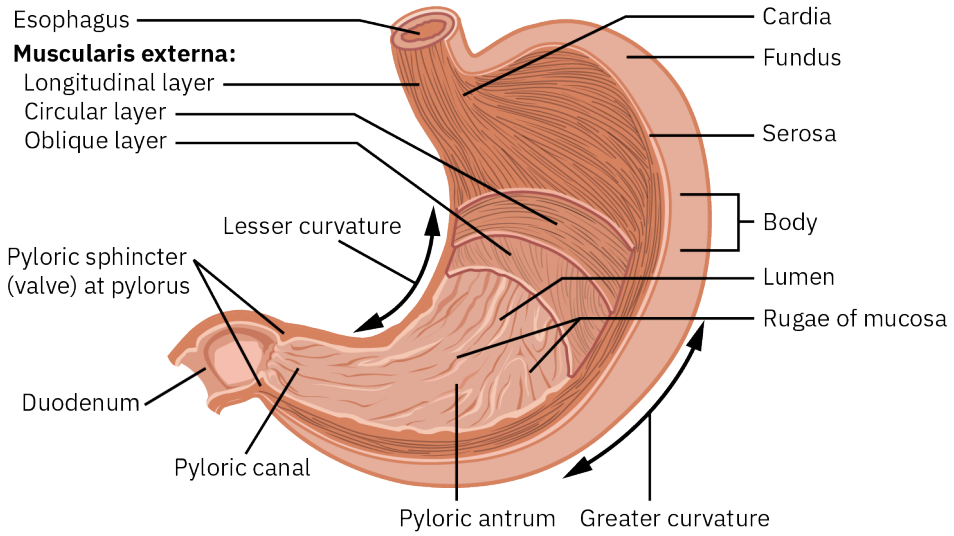


FIGURE 29.5 The stomach has four major regions: the cardia, fundus, body, and pylorus. The addition of an inner oblique smooth muscle layer gives the muscularis the ability to vigorously churn and mix food. (credit: modification of work from *Anatomy and Physiology 2e.* attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The regulation of food and fluids in the stomach is controlled by autonomic neuromuscular innervation of two sphincters: the lower esophageal sphincter (gastroesophageal sphincter) and the pyloric sphincter. The pyloric sphincter separates the stomach from the first part of the small intestine, the duodenum. Much like the upper and lower esophageal sphincters, it is also a ringlike band of smooth muscle. The pyloric sphincter opens and closes under neuromuscular automaticity to control the passage of partially digested food and stomach contents into the small intestine. A malfunctioning pyloric sphincter may lead to delayed gastric emptying, known as gastroparesis. In another type of dysfunction, the pyloric sphincter empties the gastric contents too quickly into the small intestine, causing bloating and discomfort.

The digestive process involves three phases: the cephalic phase, the gastric phase, and the intestinal phase. The cephalic phase received its name because it begins with the brain. Food is ingested in the mouth, but the experience of seeing, smelling, and tasting food involves the brain. The neurologic sensory stimulation of ingesting food and fluids stimulates the vagus nerve, the secretion of acetylcholine, and motor responses of the parasympathetic nervous system. The production of gastric acid is essential to aid digestion, absorption, and metabolism. It is regulated through neuronal and endocrine pathways (Engevik et al., 2020). Histamine, gastrin (released from G cells), and acetylcholine are substances necessary for the parietal cells to produce and release hydrochloric (HCl) acid. The stomach produces 1500–2000 mL of HCl acid daily, and an adequate amount of it is necessary for vitamin B_{12} to be extracted from food sources. In addition, intrinsic factor, which is crucial for vitamin B_{12} absorption, is produced and released by the parietal cells. The entrance of food and fluids into the stomach initiates the second phase of digestion, the gastric phase. As indicated by its name, the gastric phase takes place in the stomach.

Within the parietal cells, hydrogen–potassium (H^+-K^+) ATPase enzymes comprise the proton pump that generates and secretes HCl acid in response to acetylcholine, histamine, or gastrin binding to receptors on the parietal cells. This action increases the hydrogen ion (H^+) concentration, creating an acidic environment in the stomach that supports digestion by breaking down food, primarily carbohydrates and protein. Hydrochloric acid is also important in promoting the absorption of minerals. The acidic environment further aids digestion by controlling harmful microorganisms such as bacteria or viruses in the stomach.

The stomach acts as a basin for digestion. Stomach muscles and rugae stretch and contract in response to the volume of food in the stomach. When stretched, the rugae provide increased surface area for enhanced nutrient absorption. The upper muscles relax to let food and fluids enter the stomach; the lower muscles churn and mix food with digestive juices to form chyme and start the breakdown of proteins. Absorption of nutrients is minimal at this point, but protein digestion is further enhanced when the chief cells secrete **pepsinogen**, which is converted to pepsin. An acidic environment with a pH of 1.5–2.0 is needed for pepsin activation. The HCl acid lowers and maintains the acidic pH of the stomach.

One of the main ways the stomach keeps itself from becoming irritated by the HCl acid is by producing mucus via the goblet cells. However, the protective structure of the mucosal membrane may become eroded when exposed to excessive HCl acid and pepsin, especially if these substances permeate the epithelium. This condition is commonly referred to as **gastritis** and may lead to serious problems as the stomach lining becomes irritated and inflamed. Gastritis can be painful and impair digestion and may cause life-threatening complications, such as bleeding or perforation.

Gastric mucosal cells counteract the HCl acid by secreting prostaglandin E_2, a strong, lipid-rich molecule that stimulates gastric mucus and pancreatic bicarbonate. Prostaglandins ensure adequate submucosal perfusion. When prostaglandin E_2 is not sufficient to prevent gastritis, clients may need medications such as antacids to reduce or eliminate symptoms. Because prostaglandins play an essential role in enhancing protective features of the stomach, some medications that inhibit prostaglandin synthesis, such as ibuprofen, can injure the stomach. Nurses should instruct clients that taking too much ibuprofen can be harmful to the stomach and kidneys and can lead to bleeding due to altered platelet aggregation.

Prostaglandin E_2 also has a role in GI motility as chyme is peristaltically pushed toward the pyloric sphincter and into the duodenum for the final and third phase of digestion—the intestinal phase, which begins in the small intestine.

29.3 Introduction to the Small and Large Intestines

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 29.3.1 Describe the structure and function of the small and large intestines.
- 29.3.2 Discuss common conditions that affect the small and large intestines.

Small and Large Intestines

The largest GI organ is the small intestine (Figure 29.6). The duodenum, jejunum, ileum, and ileocecal valve comprise the almost 20 feet of the small intestine. The primary functions of the small intestine are absorption and digestion; the small intestine is responsible for 90%–95% of nutrient absorption. The muscles of the small intestine

further mix the chyme with digestive fluids for continued breakdown. The small intestine receives digestive juices from the liver, gallbladder, and pancreas. Bile acids from the liver and gallbladder enter the small intestine and break down fat for absorption in the small intestine. The pancreatic enzymes **lipase**, **protease**, and **amylase** travel through the pancreatic duct to the small intestine to facilitate digestion. Lipase, together with bile salts, breaks down fats and aids absorption of fat-soluble vitamins (A, D, E, K). Poor fat absorption may result in steatorrhea (fatty bowel movements). Protease breaks down protein for absorption. Amylase is released from the pancreas into the proximal small intestine to break down and absorb carbohydrates.

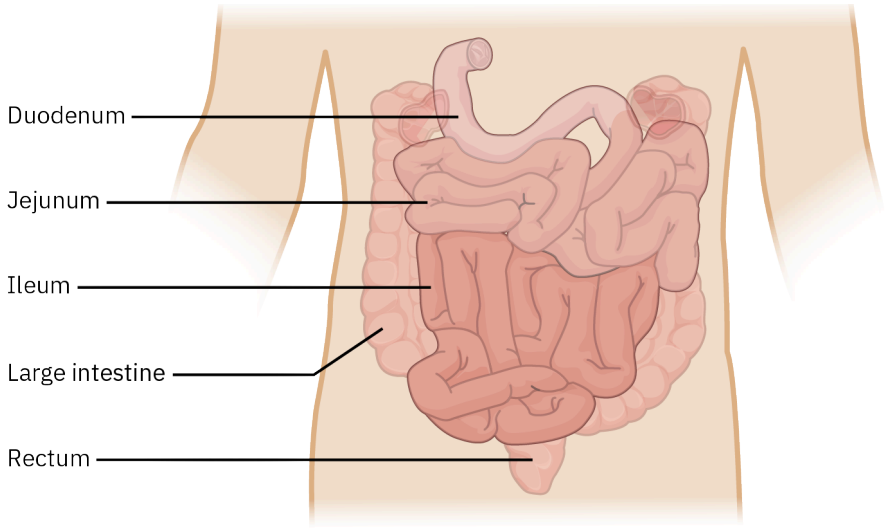


FIGURE 29.6 The three main regions of the small intestine are the duodenum, jejunum, and ileum. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Unique to the small intestine are tiny fingerlike projections called villi that line the walls of the small intestine. The villi protrude into the lumen to absorb water and nutrients into the circulatory system. The highly vascular villi line the entire small intestine to accomplish most of the digestion and absorption processes as peristalsis continues to move nutrients and digestive waste along the alimentary canal. The blood capillaries absorb carbohydrates and proteins. The lymph capillaries, also called lacteals, absorb fats. Disorders affecting the intestinal villi of the small intestine may result in malabsorption or nutritional disorders.

The large intestine, also known as the colon, receives waste products from the small intestine. Water is further absorbed from the waste products in the large intestine and forms stool. Peristaltic movements push stool toward the rectum. Under expected conditions, when waste products reach the rectum, most of the water has been reabsorbed into the body, leaving solid stool for evacuation from the body. The large intestine receives unabsorbed and undigested food material (waste products), absorbs water and electrolytes, and forms feces. The large intestine maintains over 500 species of bacteria that promote fermentation of indigestible material in the colon. The bacteria in the large intestine are responsible for absorbing vitamin K and B vitamins, including biotin (Thursby & Juge, 2017).

Irritable bowel syndrome (IBS) is a common disorder affecting the intestine. The symptoms of IBS range from mild to severe and vary from person to person. Symptoms may include bloating, gas, abdominal pain or discomfort, abdominal spasms, cramping, and constipation or diarrhea (or both). Because people experience varying types of symptoms, IBS is further categorized as IBS-C (constipation), IBS-D (diarrhea), IBS-M (mixed symptoms of diarrhea and constipation), and IBS-U (unsubtyped, with varying inconsistent symptoms). Although IBS is a chronic condition, most people with IBS can manage their disease with lifestyle changes such as consistently eating healthy, balanced meals; staying hydrated; and reducing stress.

LINK TO LEARNING

Resources from the Mayo Clinic on Irritable Bowel Syndrome (https://openstax.org/r/mayirritable)

The Mayo Clinic website (n.d.) provides a vast amount of information about IBS for health care professionals and clients, including its symptoms, causes, diagnosis, treatment (pharmacologic and nonpharmacologic), and lifestyle modifications (https://openstax.org/r/newsnetwork).

Access multimedia content (https://openstax.org/books/pharmacology/pages/29-3-introduction-to-the-small-and-large-intestines)
The Mayo Clinic also provides short videos on how IBS can affect individuals and how people can cope with it.

Table 29.2 lists common GI conditions, associated general manifestations, and drugs commonly used to treat these conditions. Table 29.3 presents common actions of digestive enzymes.

GI Conditions	Manifestations	Common Drugs Used to Treat GI Conditions
• Food or medication allergies • Adverse reaction to medications • Frequent use of nonsteroidal anti-inflammatory drugs (NSAIDs) • Food poisoning • Intestinal infections • Esophageal strictures • Celiac disease • Crohn's disease • Irritable bowel syndrome • Cholecystitis/cholelithiasis • Ulcers (peptic ulcer disease) • Gastritis • GERD • Pancreatitis • Liver disease • Polyps • Hemorrhoids • Cancer	• Bloating • Belching • Nausea • Vomiting • Dyspepsia • Heartburn • Dysphagia • Abdominal pain • Diarrhea/constipation • Bleeding • Flatus • Visceral pain	• *Antiemetics:* phenothiazines/dopamine antagonists, prokinetic agents, antihistamines, serotonin receptor antagonists, neurokinin-1 (substance P) receptor antagonists, anticholinergics, cannabinoids • *Antidiarrheals:* nonspecific drugs (e.g., opioids) and specific drugs (e.g., bismuth subsalicylate, bulk-forming agents) • *Laxatives:* bulk-forming agents (e.g., psyllium), surfactants (e.g., docusate sodium), stimulants (e.g., bisacodyl), osmotics (e.g., magnesium citrate, lactulose), lubricants (e.g., mineral oil) • *Medications for IBS:* lubiprostone for IBS-C and alosetron for IBS-D • Antacids (aluminum, magnesium, calcium, and sodium compounds) • Histamine type-2 receptor antagonists (e.g., famotidine, cimetidine) • Proton pump inhibitors (e.g., esomeprazole, omeprazole) • Pepsin inhibitors/mucosal protectants (e.g., sucralfate) • Prostaglandin-E analogs (e.g., misoprostol) • Antibiotics (e.g., amoxicillin, clarithromycin, metronidazole, tetracycline)

TABLE 29.2 **Common Gastrointestinal Conditions**

Active Site	Enzyme	Effect on Nutrients
Mouth	Salivary amylase	Breaks down starches into disaccharides
Stomach	Pepsin	Breaks down proteins into large peptides
Pancreas	Amylase	Continues the breakdown of starches
Pancreas	Chymotrypsin, trypsin	Continue the breakdown of proteins
Pancreas	Lipase	Breaks down fats into fatty acids and glycerol
Small intestine	Maltase, sucrase, lactase	Break down disaccharides into monosaccharides
Small intestine	Peptidase	Breaks down dipeptides into amino acids

TABLE 29.3 **Common Actions of Digestive Enzymes**

CLINICAL TIP

Assess for Gastrointestinal Health Practices

When taking a client's health history, nurses should ask about:

- Dietary practices: food preparation, food shopping and accessibility, healthy and unhealthy food choices, cultural or religious food preferences, meal timing, food allergies or intolerances
- Nutritional supplements: vitamins, minerals, herbal or natural supplements, need for nutritional counseling
- Oral health: dental history, tooth or gum disease, oral mucosal integrity
- Appetite: recent changes
- Preventive health: hydration habits, exercise habits, colonoscopy history
- Bowel movements: changes in patterns
- Weight: recent unintended weight gain or loss

Chapter Summary

This chapter introduced the GI system, which is essential for optimal nutrition, health, and wellness of the human body. The complex processes of ingestion, digestion, absorption, and metabolism require properly functioning GI structures. The overall process was described, from mastication of food through evacuation of stool. The chapter explained how dysfunction or physical deficits can lead to GI problems, which may be mild and temporary or may result in chronic and even life-threatening conditions. Medications are often essential to promote a healthy, functioning GI system and to augment nutrition.

Key Terms

absorption the passage of digested products from the intestinal lumen through mucosal cells and into the bloodstream or lacteals

alimentary canal the digestive tract from the mouth to the anus

amylase an enzyme in the saliva and pancreatic juice that catalyzes the breaking down of starch, glycogen, and related polysaccharides into more simple and readily usable forms of sugar

aspiration the inhalation of fluid or solid objects into the lower airways or lungs

bile alkaline solution produced by the liver and important for the emulsification of lipids

chyme the mixture of partly digested food and digestive secretions found in the stomach and small intestine during the digestion of a meal; it is a varicolored, thick, nearly liquid mass

digestion the process by which food is broken down mechanically and chemically in the gastrointestinal tract and converted to absorbable forms

epiglottis the uppermost cartilage of the larynx located immediately posterior to the root of the tongue; covers the entrance of the larynx when a person swallows and prevents food or liquids from entering the airway

gastritis acute or chronic inflammation of the stomach lining

gastroesophageal reflux disease (GERD) a common condition in which acid from the stomach (gastric and/or duodenal) flows back into the esophagus, causing discomfort and, in some instances, damage to the esophageal lining

hydrochloric (HCl) acid an inorganic acid normally present in gastric juice; destroys fermenting bacteria that might cause intestinal tract disturbances

ingestion the process of taking substances (particularly food) into the gastrointestinal tract

lipase pancreatic enzyme that breaks down triglycerides into free fatty acids and glycerol to be used in the body

lower esophageal sphincter the sphincter around the opening of the esophagus into the stomach; separates these linked organs from each other and prevents the reflux of stomach acids into the esophagus; also called the *cardiac sphincter*

mastication chewing; involves coordination of the large temporal, masseter, and pterygoid muscles as well as other smaller muscles of the mandible and tongue to grind food under the influence of the mandibular division of cranial nerve V

metabolism sum of all of the body's chemical reactions

pepsin the chief enzyme of gastric juice, which converts proteins into proteoses and peptones; formed by the chief cells of gastric glands and producing its maximum activity at a pH of 1.5–2

pepsinogen the antecedent of pepsin existing in the form of granules in the chief cells of gastric glands

peristalsis muscular contractions and relaxations that propel food through the GI tract

protease pancreatic enzyme that breaks down proteins in the diet; also provides protection from organisms that may live in the intestines, such as certain bacteria and yeast

saliva the fluid secretion of the salivary glands and oral mucous gland that begins the process of food digestion; moistens food for tasting, chewing, and swallowing; initiates digestion of starches; moistens and lubricates the mouth; acts as a solvent for excretion of waste products; also known as spit or spittle

upper esophageal sphincter a sphincter that keeps the opening between the posterior pharynx and the proximal esophagus closed, except during swallowing; maintained principally by the cricopharyngeal muscle

Review Questions

1. The nurse is caring for a client with inflammation of the biliary duct. The nurse anticipates that the client will need to limit dietary intake of which nutrient?

a. Fats
b. Proteins
c. Carbohydrates
d. Fiber

2. A nurse is developing a care plan for a client with gastritis. Which potential complication should the nurse address?
a. Jaundice
b. Bleeding
c. Acute renal failure
d. Thromboembolism

3. During the health history of a client who had radiation to the head and neck for cancer, the client informs the nurse that their salivary glands were damaged. Which assessment finding should the nurse anticipate?
a. Moist buccal membranes
b. Difficulty swallowing
c. Altered speech
d. Constipation

4. The nurse is caring for a client with dysfunction of the upper esophageal sphincter. Which sign or symptom would the nurse expect the client to have?
a. Early fullness after eating
b. Heartburn
c. Aspiration of food
d. Vomiting

5. The nurse is preparing a client for discharge following a small bowel resection because of cancer. Which instruction should the nurse include in the discharge education?
a. Take daily liquid vitamin and mineral supplements.
b. Limit daily fluid intake.
c. Avoid starchy foods.
d. Take a laxative for constipation.

6. The nurse is caring for a client with insufficient lipase production. The nurse explains to the client that absorption of which vitamin will be impaired?
a. Folate
b. Vitamin B_{12}
c. Vitamin K
d. Thiamine

7. The nurse is providing education to a client with a newly diagnosed condition related to dysfunctional villi of the small intestine. Which of the following can result from this condition?
a. Esophageal varices
b. Heartburn
c. Gastritis
d. Nutritional deficiencies

8. When assessing a client's gastrointestinal health, which question should the nurse ask?
a. "Do you have problems walking?"
b. "Have you had an unintended weight gain or loss?"
c. "Do you have any drug allergies?"
d. "How many hours do you sleep each night?"

9. The nurse is assessing a client with damage to cranial nerve VII (the facial nerve). Which finding does the nurse expect to see in this client?
   a. Difficulty swallowing
   b. Problems with chewing
   c. Impaired salivation
   d. Vocal cord atrophy

10. Which medication does the nurse anticipate will be ordered for a client admitted with a diagnosis of gastritis?
   a. Antacids
   b. Nonsteroidal anti-inflammatory drugs (NSAIDs)
   c. Aspirin
   d. Antiemetics

CHAPTER 30
Gastrointestinal Disorder Drugs

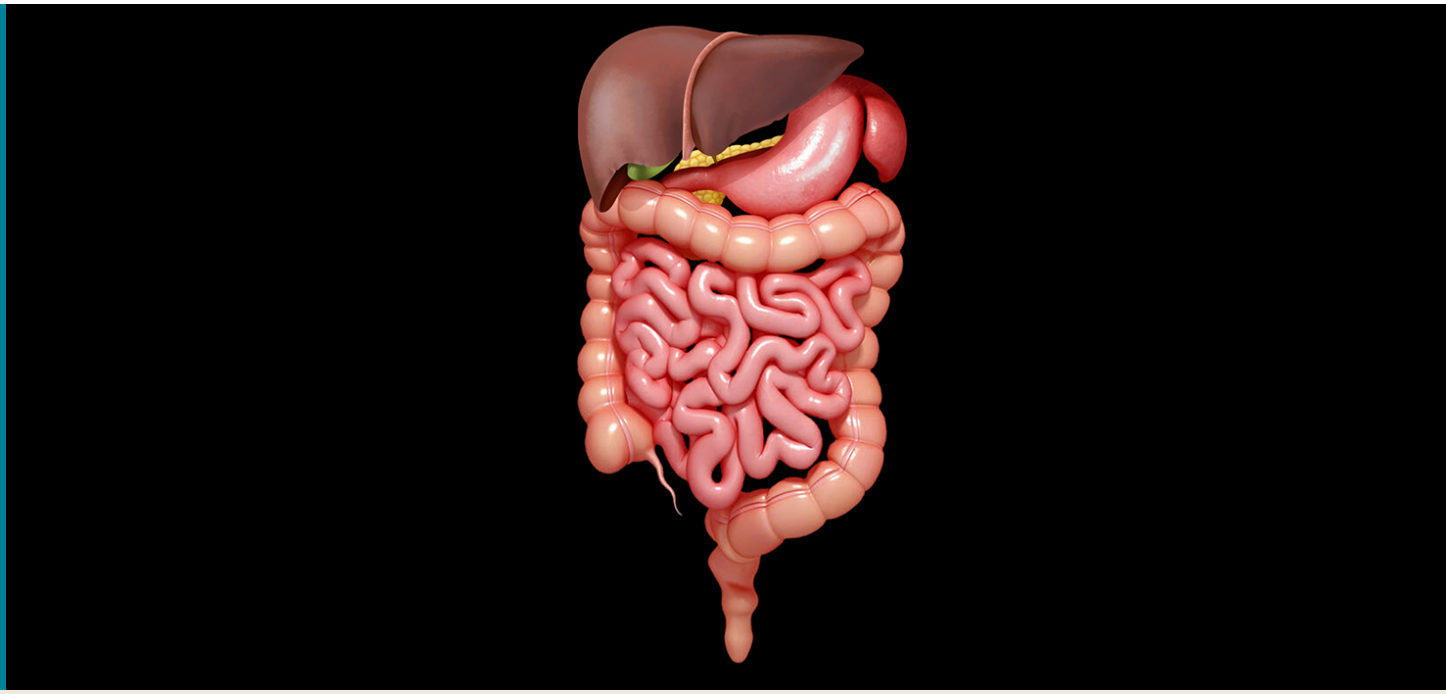


FIGURE 30.1 The digestive system breaks down food into nutrients that can be absorbed into the bloodstream to give the body energy and the ability to grow and repair itself. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The normal function of the gastrointestinal (GI) system is regulated and controlled by the central nervous system. The parasympathetic and sympathetic nervous systems play a role in gastrointestinal muscle movements, tone, motility, and mucosal secretions, especially in the stomach and esophagus. The nature of the gastrointestinal and neuronal relationships makes the GI system susceptible to conditions causing symptoms such as nausea, vomiting, diarrhea, and constipation. In this chapter, drugs used to treat and manage these symptoms will be discussed.

30.1 Antiemetics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 30.1.1 Identify the characteristics of antiemetic drugs used to treat gastrointestinal disorders.
- 30.1.2 Explain the indications, actions, adverse reactions, and interactions of antiemetic drugs used to treat gastrointestinal disorders.
- 30.1.3 Describe nursing implications of antiemetic drugs used to treat gastrointestinal disorders.
- 30.1.4 Explain the client education related to antiemetic drugs used to treat gastrointestinal disorders.

Antiemetics are a group of drugs that manage nausea and vomiting. They are classified by mechanism of action and receptor target. Generally, antiemetics work by reducing the hyperactivity of the vomiting reflex in the brain, either locally or centrally, by modulating neurotransmitter receptor sites. Localized antiemetics, such as antacids, work at the site of acid production, thereby decreasing the response to excessive acid stimulation that may induce vomiting.

Conversely, centrally acting antiemetics directly block the **chemoreceptor trigger zone (CTZ)** or suppress the **vomiting center (VC)**.

CLINICAL TIP

Identify Underlying Factors Contributing to Nausea and Vomiting

When administering an antiemetic, the health care provider should identify the factors causing nausea and vomiting. Treatment or elimination of the causative factors should be a goal of antiemetic treatment.

Phenothiazines

Phenothiazines are a class of drugs that produce antiemetic, antipsychotic, antihistaminic, and anticholinergic effects, primarily acting centrally to alleviate mild to moderate nausea and vomiting resulting from anesthesia, surgery, radiation, or chemotherapy. They work by blocking dopamine receptors in the brain's chemoreceptor trigger zone (CTZ), effectively countering nausea and vomiting, so they are classified as dopamine antagonists. Additionally, phenothiazines interact with alpha adrenergic, serotonergic, histaminic, and muscarinic receptors, potentially causing orthostatic hypotension and sedation. Prioritizing fall precautions is essential in the nursing plan of care when administering these drugs. See Table 30.1.

Promethazine

Promethazine, a widely used phenothiazine, effectively manages nausea, motion sickness, and pregnancy-induced nausea and vomiting when other treatments are ineffective. Its antiemetic effects are attributed to depressing the CTZ. It also possesses antiserotonin, anticholinergic, and local anesthetic properties, resulting in moderate to significant sedative effects. Promethazine is also considered an antihistamine and antivertigo agent, making it versatile in allergy symptoms, allergic reactions, and pre- and postoperative sedation for adults and children over age 2.

Prochlorperazine

Prochlorperazine is another commonly used phenothiazine to manage severe nausea and vomiting, including those associated with chemotherapy or radiation therapy. Prochlorperazine suppresses the CTZ and blocks postsynaptic dopamine receptors, making the drug an effective antiemetic and antipsychotic.

Chlorpromazine

Chlorpromazine is a phenothiazine derivative that widely affects the central nervous system, producing antiemetic and antipsychotic effects. It is primarily used as an antiemetic, targeting the CTZ to manage mild to moderate nausea and vomiting. Other uses include intractable hiccups, bipolar disorder, schizophrenia, attention-deficit hyperactivity disorder, and tetanus as an adjunct drug. However, its dopamine receptor blockade can lead to extrapyramidal symptoms, making it less commonly used for nausea and vomiting compared to promethazine and prochlorperazine. See Table 30.2 for additional information on chlorpromazine.

FDA BLACK BOX WARNING

Chlorpromazine and Prochlorperazine

Increased mortality can occur when taking chlorpromazine and prochlorperazine in older adults with dementia-related psychosis.

Promethazine

Severe respiratory depression and death in pediatric clients under age 2 may occur with promethazine.

Antihistamines

Antihistamines are a class of medications that are commonly used to treat allergic reactions and upper respiratory conditions, but they also serve as antiemetics. Antihistamines, known as H_1-receptor antagonists, compete with the H_1-receptor sites in various body tissues, including mucous membranes, arterioles, capillaries, and the vomiting

center (VC). By doing so, they effectively block muscarinic and histaminergic receptors, making them effective antiemetics. See Table 30.1.

Hydroxyzine

Hydroxyzine, a first-generation antihistamine and H_1-receptor antagonist, effectively treats nausea and vomiting caused by anesthesia, motion sickness, or pregnancy. It also acts as an anticholinergic by counteracting excessive acetylcholine at the cholinergic receptors at the CTZ and VC, which receive signals from the inner-ear vestibular network. Hydroxyzine is available various forms, including tablets, capsules, oral solutions, and injectables. When using the injectable form of hydroxyzine to treat nausea and vomiting, it should be administered deep into a large muscle, such as the gluteus maximus for adult clients and the vastus lateralis (the muscle on the outside of the thigh) for pediatric clients.

Meclizine

Meclizine, a first-generation antihistamine with anticholinergic properties, is used as an antiemetic and antivertigo agent. It acts by reducing excitability in the inner-ear labyrinth and vestibular simulation, thereby affecting the CTZ and providing relief from vertigo and nausea. Meclizine is used to manage nausea and vomiting associated with motion sickness or diseases affecting the vestibular system. It is available in oral tablet form, with an onset of about 60 minutes. The drug is readily available from the GI tract and has a duration of action of 8–24 hours.

Serotonin Receptor Antagonists

Serotonin (5-HT_3) receptor antagonists prevent emesis by blocking the serotonin receptors centrally located within the CTZ. These agents exhibit their antiemetic action by impeding peripheral serotonin receptors on the afferent vagal neurons, which transmit signals from the upper GI tract to the CTZ, thereby mitigating nausea and vomiting. See Table 30.1.

Ondansetron

Ondansetron acts by inhibiting the serotonin receptors and preventing activation of the vomiting reflex. Ondansetron is one of the most effective antiemetics used to treat postoperative nausea and vomiting as well as nausea and vomiting associated with chemotherapy and radiation therapy. Additionally, it has been used off-label for treating conditions such as hyperemesis gravidarum, alcohol dependence, and pruritis.

Granisetron

Granisetron is a serotonin receptor antagonist like the prototype ondansetron. Granisetron is available as a tablet, oral solution, transdermal patch, and solution for injection. It is used to prevent and/or treat chemotherapy-induced nausea and vomiting. Oral granisetron is administered 1 hour before chemotherapy. The transdermal granisetron patch is applied 24–48 hours before chemotherapy and remains in place for up to 7 days.

Substance P/Neurokinin-1 (NK1) Receptor Antagonists

Substance P is a neurotransmitter found in high concentrations in the central and peripheral nervous systems that plays a vital role in pain modulation and may influence vomiting via the neurokinin-1 (NK_1) receptors. Neurokinin-1 antagonists block the effects of substance P in the CNS and are effective in treating chemotherapy-induced and postoperative nausea and vomiting. The primary goal of these antagonists is to prevent nausea and vomiting by inhibiting substance P. As substance P coexists with serotonin in the body, the NK_1 antagonist works best when concurrently used in combination with a serotonin antagonist and glucocorticoid. See Table 30.1.

Aprepitant

Aprepitant, a substance P/NK_1 receptor antagonist, crosses the blood-brain barrier to block neurokinin action in the CTZ, with peripheral effects in the GI tract to combat nausea and vomiting. Often used concurrently with ondansetron, aprepitant may be administered by mouth or intravenously to enhance the antiemetic activity of the serotonin antagonist for acute and delayed effects of vomiting caused by chemotherapeutic agents.

Rolapitant

Rolapitant is a tablet that blocks the action of substance P and neurokinin to prevent nausea and vomiting in chemotherapy-induced nausea and vomiting. Rolapitant prevents both acute and delayed chemotherapy-induced nausea and vomiting. Nursing assessment includes monitoring for drug effectiveness by emetic control.

Anticholinergics

Anticholinergics, also called *cholinergic antagonists*, are drugs that block the actions of acetylcholine. Motion sickness, nausea, and vomiting may be caused by excessive acetylcholine at the CTZ and vestibular receptors in the VC. Anticholinergics are often used as antiemetics, as they interfere with or block inner-ear nerve impulses to the VC that causes vomiting.

Scopolamine

Scopolamine is a transdermal application with a controlled release system to prevent nausea and vomiting associated with motion sickness and anesthesia. Scopolamine inhibits the action of acetylcholine on nerves that connect the vestibular apparatus of the inner ear to the VC smooth muscle. Scopolamine transdermal patch is generally administered 4 hours before traveling in clients who suffer from motion sickness and in clients with post-anesthesia nausea and vomiting. Other routes of administration include oral and subcutaneous.

Application of the transdermal patch is best to the hairless area behind the ear, after the area is cleansed and dried to ensure adherence (see Figure 30.2). Nurses should wear gloves during application to avoid accidental cross-absorption and should educate clients not to touch the patch. It is often recommended that the patch be covered with a bandage or medical tape to avoid accidental cross-absorption. The patches are replaced every 3 days as needed. When removing the transdermal patch, nurses should wear gloves and fold the patch in half so that the adhesive sides stick together for disposal, following facility policy. Nurses should wash hands thoroughly after handling scopolamine.

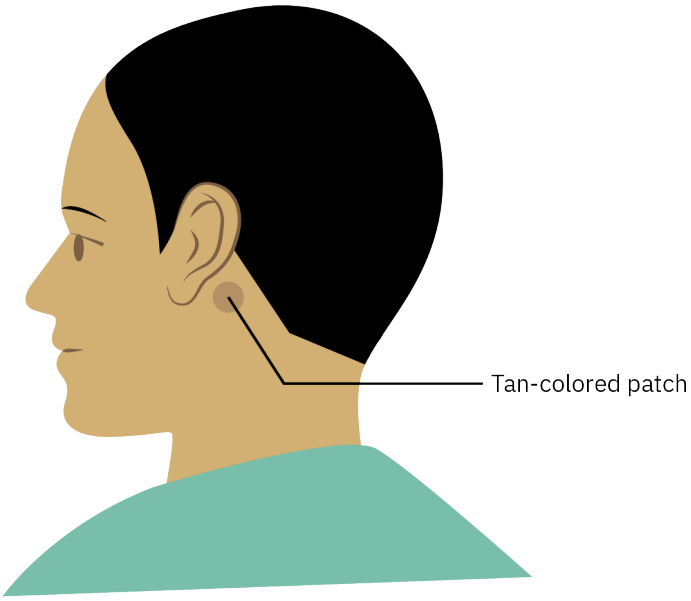


FIGURE 30.2 The scopolamine patch is best applied to the hairless area behind the ear. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Cannabinoids

Cannabinoids are a group of ingredients found in *Cannabis sativa* plant, commonly referred to as cannabis. They interact with the endocannabinoid system, influencing nausea and vomiting regulation. Notably, delta-9-tetrahydrocannabinol (THC) exhibits antiemetic properties by binding to CB1 and CB2 receptors in the brain and GI tract, reducing signals associated with nausea and vomiting. This makes cannabinoids valuable in managing conditions like chemotherapy-induced nausea and vomiting.

LINK TO LEARNING

Medical Marijuana (https://openstax.org/r/mayoclinicorgh)

The Mayo Clinic has published an article that discusses medical marijuana, also known as medical cannabis, which is legal in some U.S. states and used to treat pain, nausea, and other symptoms. Research supports the

use of medical cannabis to treat several conditions, including severe nausea or vomiting caused by cancer treatment.

Dronabinol

Dronabinol is a synthetic form of delta-9-tetrahydrocannabinol (THC) that manages chemotherapy-induced nausea and vomiting (CINV) by activating cannabinoid receptors in the brain. This activation helps regulate the body's response to nausea and vomiting, reducing their intensity. Additionally, dronabinol is used to stimulate appetite in conditions like HIV- and AIDS-related anorexia and cachexia (wasting syndrome). See Table 30.1.

Table 30.1 lists common antiemetics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Phenothiazines	
Promethazine (Phenergan)	*Oral/rectal/intramuscular/intravenous (IV):* 12.5–25 mg every 4–6 hours.
Chlorpromazine (Compro)	*Oral:* 10–25 mg every 4–6 hours. *Intramuscular/IV:* 25–50 mg every 3–4 hours.
Prochlorperazine (Compazine)	*Oral/intramuscular:* 5–10 mg 3–4 times daily. Maximum dose: 40 mg/day. *IV:* 2.5–10 mg 3–4 times daily. Maximum dose: 10 mg/dose or 40 mg/day. *Rectal:* 25 mg every 12 hours.
Antihistamines	
Hydroxyzine (Vistaril)	*Oral/intramuscular:* 25–100 mg every 4–6 hours.
Meclizine (Antivert)	*Oral:* 25–50 mg 1 hour before travel. May repeat once every 24 hours.
Serotonin Receptor Antagonists	
Ondansetron (Zofran)	*Oral:* 8 mg 30 minutes before chemotherapy; repeat every 8 hours if needed. *Intramuscular:* 4 mg undiluted. *IV:* 4 mg undiluted over 2–5 minutes.
Granisetron (Kytril)	*IV:* 10 mcg/kg infused starting 30 minutes before chemotherapy; repeat at 4 and 8 hours. *Oral:* 1 mg twice daily (1 mg 1 hour before chemotherapy, second dose 12 hours later). *Transdermal patch (each patch releases 3.1 mg of granisetron per 24 hours):* 1 patch every 7 days.
Neurokinin-1 Receptor Antagonists	
Aprepitant (Emend, Cinvanti)	*Oral:* Initial dose 3 mg/kg up to a maximum dose of 125 mg 1 hour before chemotherapy, then 80 mg every morning for the next 2 days in conjunction with other antiemetics. *IV:* 100–130 mg 20 minutes before chemotherapy.
Rolapitant (Varubi)	*Oral:* 180 mg single dose 1–2 hours before chemotherapy.
Anticholinergics	
Scopolamine (Transderm-Scop)	*Transdermal patch (each patch contains 1 mg of scopolamine):* Apply patch to skin in the post-auricle area for use up to 3 days.
Cannabinoids	
Dronabinol (Marinol)	*Oral:* 5 mg administered 1–3 hours prior chemotherapy, then every 2–4 hours after chemotherapy, for a total of 4–6 doses per day. Maximum dose: 15 mg per dose, 4–6 doses per day.

TABLE 30.1 **Drug Emphasis Table: Antiemetics** (source: https://dailymed.nlm.nih.gov/dailymed/; Mayo Foundation for Medical Education and Research, 2023b)

Adverse Effects and Contraindications

Typical adverse effects of common antiemetics include drowsiness, fatigue, dry mouth, constipation, headache, and dizziness. Some antiemetics such as chlorpromazine may cause **extrapyramidal symptoms** including dystonia, Parkinson-like symptoms, and tardive dyskinesia, particularly with long-term use.

Certain antiemetics, such as dronabinol, should be used cautiously during pregnancy and when breastfeeding, as they may have adverse effects on fetal development and neurodevelopment outcomes.

Antiemetics should be used cautiously or avoided when used concomittantly with other CNS depressants, as this may cause increased risk for CNS effects such as enhanced sedation, respiratory depression, and impaired cognitive function. The age of the client should be carefully considered prior to administering antiemetics, specifically in older adults and pediatric clients due to their potential adverse effects.

Contraindications for antiemetics include hypersensitivity to the drug or any of its components.

Table 30.2 is a drug prototype table for antiemetics featuring chlorpromazine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Phenothiazine; dopamine antagonist **Mechanism of Action** Suppresses the chemoreceptor trigger zone (CTZ) and blocks the postsynaptic dopamine receptors in the brain, causing an antiemetic effect	**Drug Dosage** *Oral:* 10–25 mg every 4–6 hours. *Intramuscular/IV:* 25–50 mg every 3–4 hours.
Indications Nausea and vomiting Psychotic disorders **Therapeutic Effects** Prevents/reduces nausea and vomiting Antipsychotic	**Drug Interactions** CNS depressants Anticonvulsants Oral anticoagulants Phenytoin Propranolol Thiazide diuretics Alcohol **Food Interactions** No significant interactions
Adverse Effects Neuroleptic malignant syndrome Tardive dyskinesia Orthostatic hypotension Drowsiness Jaundice Hematologic disorders (leukopenia agranulocytosis, hemolytic anemia, pancytopenia) Hypotension Electrocardiogram (ECG/EKG) changes (Q- and T-wave distortions) Dry mouth Constipation Urinary retention	**Contraindications** Hypersensitivity to phenothiazines Comatose states Concurrent use of CNS depressants (alcohol, barbiturates, narcotics, etc.) Caution: Older clients with dementia-related psychosis treated with antipsychotic drugs and chlorpromazine are at an increased risk of death

TABLE 30.2 **Drug Prototype Table: Chlorpromazine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antiemetics:

- Prior to administering, assess the client's medical history, current drug list, and allergies.
- Educate the client regarding antiemetic effects, such as dry mouth, constipation, hypotension, and urinary retention.
- Moitor vital signs for signs of hypotension and respiratory depression, as these medications may cause CNS depression.
- Monitor urine input and output for urinary retention.
- Monitor the client closely for extrapyramidal effects such as dystonia, Parkinson-like symptoms, and tardive dyskinesia. Report these to the health care provider immediately.
- Initiate fall precautions due to the adverse effects of orthostatic hypotension and dizziness.
- Provide oral care and lozenges or saliva substitute for dry mouth.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antiemetic should:

- Use sugarless candy, gum, or a saliva substitute for dry mouth as this is a normal side effect of these drugs.
- Increase their dietary intake of fiber and increase fluid intake, if not contraindicated, to help reduce the risk of constipation.
- Monitor blood pressure and report systolic blood pressure less than 90 mmHg and diastolic pressure less than 60 mmHg to the health care provider as this may represent hypotension.
- Rise from a lying to sitting or sitting to standing position slowly as these drugs may cause dizziness and orthostatic hypotension.
- Report signs of muscle contractions, tremors, ataxia, involuntary facial movements, or difficulty controlling movement as these may be symptoms of serious adverse effects of the drugs.

The client taking an antiemetic *should not:*

- Take these drugs with alcohol or other CNS depressants because this may cause increased depression of the central nervous system, resulting in drowsiness, dizziness, and respiratory depression.
- Drive or operate heavy machinery because these drugs may cause drowsiness or dizziness.

30.2 Antidiarrheals

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 30.2.1 Identify the characteristics of antidiarrheal drugs used to treat gastrointestinal disorders.
- 30.2.2 Explain the indications, actions, adverse reactions, and interactions of antidiarrheal drugs used to treat gastrointestinal disorders.
- 30.2.3 Describe nursing implications of antidiarrheal drugs used to treat gastrointestinal disorders.
- 30.2.4 Explain the client education related to antidiarrheal drugs used to treat gastrointestinal disorders.

Diarrhea involves frequent, loose, watery stools. Diarrhea can be acute (lasting 1–2 days, often due to microorganisms, viruses, or food intolerance) or chronic (lasting weeks, indicating underlying conditions like IBS or Crohn's disease) (Johns Hopkins Medicine, 2023). Symptoms may include abdominal distress, cramping, bloating, nausea, and urgency. Dehydration is a serious concern, and bloody stools should be reported. **Antidiarrheal** treatments aim to slow intestinal motility, but they should not be taken if signs of infection (fever, severe pain, bloody/mucus stool) are present, as they could allow pathogens to multiply. In these cases, it is important to contact the health care provider.

CLINICAL TIP

Acute versus Chronic Diarrhea

Diarrhea is one of the most common complaints in the United States. Although the diarrheal stools of chronic versus acute diarrhea may appear similar, it is important to understand the different causes and complications of these two medical conditions. Read this online article from the American College of Gastroenterology (https://openstax.org/r/giorgtopics) to learn more.

Opioid-Related Antidiarrheal Medications

Opioid-related antidiarrheal medications activate opioid Mu-receptors in the GI tract to slow intestinal motility, allowing more time for absorption of fluid and electrolytes by the colonic mucosal. Identifying the underlying cause of the diarrhea is recommended before treating it with an antidiarrheal agent. Caution should be exercised with opioid-related antidiarrheals because, if taken at high doses, clients may experience the typical opioid effects of euphoria or CNS depression. See Table 30.3.

Diphenoxylate with Atropine Sulfate

Diphenoxylate is a synthetic narcotic that reduces intestinal movement by targeting opioid receptors, effectively stopping diarrhea. It also slightly reduces fluid and electrolyte secretion in the intestines, promoting drug absorption. However, unlike typical opioids, it lacks analgesic effects and does not affect the central nervous system (CNS) at recommended doses for diarrhea. However, when used at higher doses or over an extended period, it can lead to euphoria, sedation, and addiction, classifying it as a Schedule II drug under the Controlled Substances Act (CSA) when prescribed alone (National Library of Medicine, 2022). When combined with atropine sulfate, it produces anticholinergic side effects when higher doses are used and is classified as a Schedule V drug.

To prevent abuse, low doses of atropine, an anticholinergic, are added to diphenoxylate. Although this combination effectively manages diarrhea, atropine can lead to unpleasant side effects such as blurred vision, urinary retention, dry mouth, constipation, and tachycardia. The addition of atropine counteracts the potential euphoria from diphenoxylate, making the combination a Schedule V drug under the CSA. See Table 30.4 for additional information on diphenoxylate with atropine sulfate.

Loperamide

Loperamide is an effective antidiarrheal agent that prolongs transit time in the colon by directly inhibiting the peristatic activity of the circular and longitudinal muscles of the intestine, thereby decreasing intestinal fluid secretion into the intestinal lumen. This helps to increase the absorption of water and electrolytes in the intestines, resulting in firmer stools and a reduction in diarrhea.

Loperamide is often used for the symptoms of acute diarrhea, such as traveler's diarrhea or viral gastroenteritis. It can also be used to manage chronic diarrhea associated with conditions like inflammatory bowel disease and irritable bowel syndrome.

CLINICAL TIP

Dehydration

When administering antidiarrheals, the nurse should assess the client for signs and symptoms of dehydration by checking daily weights, skin turgor, and vital signs.

Adjuvant Antidiarrheals

Many clients experience diarrhea secondary to chemotherapeutic agents. Chemotherapy targets rapidly dividing cancer cells. However, chemotherapy often affects the cells within the gastrointestinal tract. Diarrhea caused by chemotherapy is referred to as chemotherapy-related diarrhea (CRD). Adjuvant antidiarrheals are often used for CRD to slow and manage the diarrhea (Krishnamurthi & Macaron, 2022). See Table 30.3.

Bismuth Subsalicylate

Bismuth subsalicylate (BSS) is an insoluble salt of salicylic acid and trivalent bismuth antidiarrheal that inhibits the synthesis of prostaglandins and cyclooxygenase that are responsible for inflammation and gastrointestinal motility. Bismuth subsalicylate works directly on the intestinal mucosa as a protective agent, decreasing intestinal secretions, and possesses anti-infective properties for acute diarrhea. However, pending the suspicious organisms, targeted anti-infective therapy may be necessary.

BSS is commonly used for traveler's diarrhea. It can also provide temporary relief for dyspepsia and is sometimes part of *Helicobacter pylori* (*H. pylori*) treatment alongside a proton pump inhibitor, tetracycline, and metronidazole due to its anti-inflammatory effects. BSS is available in various forms for oral administration. Chewable tablets should be crushed and taken with water. Shake liquid suspensions well before use.

Octreotide

Octreotide is a somatostatin analog primarily used for hyperpituitarism disorders, such as acromegaly. However, octreotide is an adjuvant antidiarrheal to treat several severe diarrheal conditions associated with carcinoid tumors, vasoactive intestinal polypeptide (VIP) tumors, gastrin-secreting tumors, and short bowel syndrome (Novartis, 2021). Octreotide is recommended for clients with CRD that does not respond to loperamide (Krishnamurthi & Macaron, 2022).

This long-acting octapeptide mimics somatostatin and suppresses the secretion of various hormones and peptides. Octreotide promotes fluid and electrolyte absorption in the GI tract, slowing down intestinal transit time.

Octreotide is available in capsule form for oral administration and as a parenteral solution for subcutaneous, intramuscular, or intravenous administration (DailyMed, *Octreotide acetate,* 2023). The oral route is not indicated for the treatment of diarrhea (DailyMed, *Mycapssa,* 2023). Clients who have responded well to octreotide injections may switch to intramuscular depot injections (i.e., in the buttocks), avoiding the deltoid muscle due to potential discomfort at the injection site (Novartis, 2021).

Pancreatin

Pancreatin, a medication containing porcine digestive enzymes, is used when the pancreas cannot produce essential enzymes (lipase, amylase, and protease) that are required for proper digestion of fats, carbohydrates, and proteins. Incomplete digestion occurs with deficient pancreatic enzyme levels and may cause excessive diarrhea. Pancreatic enzymes are sometimes used as a secondary treatment in conditions with excessive diarrhea.

Pancreatin is an oral medication available by prescription as a tablet or capsule or over the counter as a dietary supplement. As a digestive enzyme, pancreatin is always taken with food and with a full glass of water. Pancreatin should be immediately swallowed whole to avoid irritation to the oral mucosa. It cannot be crushed or chewed. To be effective, pancreatin must be taken consistently for the best results.

Table 30.3 lists common antidiarrheals and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Opioid-Related Antidiarrheals	
Diphenoxylate with atropine (Lomotil)	*Oral (each tablet contains 2.5 mg diphenoxylate hydrochloride and 0.025 mg of atropine sulfate)*: 2 tablets 4 times daily. Maximum dose: 20 mg per day. After initial control has been achieved, dosage may be reduced. If symptom relief is not observed within 10 days, discontinue use because symptoms are unlikely to be controlled by further use.
Loperamide (Imodium)	*Oral:* 4 mg after the first loose stool, 2 mg after each subsequent loose stool, but no more than 8 caplets in 24 hours.
Adjuvant Antidiarrheals	

TABLE 30.3 **Drug Emphasis Table: Antidiarrheals** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Bismuth subsalicylate (Pepto Bismol, Kaopectate)	*Oral:* 524 mg every 30–60 minutes as needed; no more than 8 doses in 24 hours.
Octreotide (Sandostatin)	*Subcutaneous:* 200–300 mcg per day in 2–4 divided doses for 2 weeks.
Pancreatin (Creon, Pancrelipase)	*Oral:* 5 granules 3 times daily or as recommended by the health care provider.

TABLE 30.3 **Drug Emphasis Table: Antidiarrheals** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Typical adverse effects of common antidiarrheals include constipation, nausea and vomiting, dry mouth, dizziness, drowsiness, and changes in bowel habits including the passage of harder or less-frequent stools. Antidiarrheals should be usedcautiously with monoamine oxidase inhibitors (MAOIs) and CNS depressants.

Use of diphenoxylate hydrochloride with atropine sulfate in higher doses than prescribed may lead to opioid and/or **anticholinergic effects** such as hyperthermia, flushing, tachycardia, hypotonia, lethargy, hallucinations, and repiratory depression.

Contraindications for antiemetics include hypersensitivity to the drug or any of its components.

Table 30.4 is a drug prototype table for antidiarrheals featuring diphenoxylate with atropine sulfate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antidiarrheal **Mechanism of Action** Reduces peristaltic activity and motility by inhibiting mucosal receptors responsible for peristatic reflexes, thereby stopping or reducing diarrhea	**Drug Dosage** *Oral (each tablet contains 2.5 mg diphenoxylate hydrochloride and 0.025 mg of atropine sulfate):* 2 tablets 4 times daily. Maximum dose: 20 mg per day. After initial control has been achieved, dosage may be reduced. If symptom relief is not observed within 10 days, discontinue use as symptoms are unlikely to be controlled by further use.
Indications Adjunctive therapy in management of diarrhea **Therapeutic Effects** Reduces or stops diarrhea	**Drug Interactions** MAOIs CNS depressants Alcohol **Food Interactions** No significant food interactions
Adverse Effects Drowsiness Sedation Dry mouth Urinary retention Constipation Blurred vision Nausea/vomiting Miosis (pupil constriction) Headache Dizziness Nervousness Paralytic ileus (impairment of the motor activity of the bowel)	**Contraindications** Hypersensitivity to diphenoxylate or atropine Diarrhea associated pseudomonas enterocolitis Obstructive jaundice Pediatric clients under age 6 Caution: May cause atropinism; monitor for hyperthermia, tachycardia, flushing, and dry mucous membranes

TABLE 30.4 **Drug Prototype Table: Diphenoxylate with Atropine Sulfate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antidiarrheals:

- Prior to administering, assess the client's medical history, current drug list, and allergies.
- Educate the client regarding adverse effects, such as constipation, urinary retention, blurred vision, drowsiness, and dizziness.
- Mointor vital signs and for signs of dehydration such as poor skin turgor, reduced or dark urine, tachycardia, and dry mucous membranes.
- Monitor urine input and output for urinary retention.
- Initiate fall precautions due to the adverse effects of drowsiness and dizziness.
- Provide oral care and lozenges or saliva substitute for dry mouth.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antidiarrheal should:

- Use sugarless candy, gum, or a saliva substitute for dry mouth because this is a normal side effect of these drugs.
- Report adverse effects such as blurred vision, dry mouth, drowsiness, or constipation to the health care provider.

- Report signs of abdominal distention, severe abdominal pain, fever, palpitations, or bloody diarrhea to the health care provider immediately as these may represent serious adverse effects.

The client taking an antidiarrheal *should not:*

- Use caffeine products during diarrhea episodes, as caffeine increases GI motility.
- Drive or operate heavy machinery because these drugs may cause drowsiness or dizziness.

30.3 Laxatives and Stool Softeners

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 30.3.1 Identify the characteristics of laxative and stool-softener drugs used to treat gastrointestinal disorders.
- 30.3.2 Explain the indications, actions, adverse reactions, and interactions of laxative and stool-softener drugs used to treat gastrointestinal disorders.
- 30.3.3 Describe nursing implications of laxative and stool-softener drugs used to treat gastrointestinal disorders.
- 30.3.4 Explain the client education related to laxative and stool-softener drugs used to treat gastrointestinal disorders.

Constipation is an unpleasant symptom or disorder that results in difficult stool evacuation or irregular and inconsistent stool passage, with common complaints like straining, incomplete or difficulty passing stools, or not defecating for a prolonged time. Stool may be small, round, hard, and lumpy when evacuated. Occasional constipation results in a feeling of fullness and wide-ranging discomfort. It often results from low fiber intake, dehydration, and a sedentary lifestyle. Certain medications can also promote constipation, such as anticholinergics and opioids.

Treatment involves increasing fiber intake, staying hydrated, and being physically active. Laxatives and stool softeners can help if constipation persists, but they should be used briefly to avoid dependency.

Bulk-Forming Laxatives

Bulk-forming **laxatives** relieve constipation within 24–72 hours by supplying the colon with an increase in dietary fiber. However, it is imperative that these products are taken with an adequate amount of water. If these products are not taken with enough water, it may result in worsening constipation as well as esophageal and/or stomach obstruction. Bulk-forming laxatives are commonly marketed over the counter as a fiber supplement to promote regularity and improve cardiovascular and digestive health. Bulk-forming laxatives should not be used in clients with symptoms of acute appendicitis, esophageal stricture or perforation, GI obstruction, or ileus. See Table 30.5 for adult dosing of these drugs.

Psyllium

Psyllium is an oral bulk-producing laxative that promotes natural elimination by absorbing water into its soluble fiber, softening feces and increasing stool bulk. It is considered safe and can help with occasional and chronic constipation relief. Psyllium supports digestive health, helps to maintain healthy glycemic control, promotes a healthy heart with cholesterol reduction, and promotes a healthy weight by reducing hunger (Proctor & Gamble, 2022). It is available over the counter in granules or powder to mix with water or juice. It is crucial to drink enough fluids to prevent complications like obstruction. Psyllium is also available as a wafer, but adequate water intake is essential to avoid choking and ensure its effectiveness. See Table 30.6 for additional information.

Methylcellulose

Another bulk-forming laxative, methylcellulose, is often used for both constipation and diarrhea for adults and children over age 3. Methylcellulose has also been used to promote regularity in irritable bowel syndrome (IBS) when taken as directed in capsule or powder suspension. As with its prototype, psyllium, it may take up to 3 days to work. Taking methylcellulose with several glasses of water will increase its effectiveness.

Calcium Polycarbophil

Calcium polycarbophil restores a balanced moisture level in the colon to form solid soft stool in cases of constipation or diarrhea. It promotes GI motility and regularity in conditions such as acute bowel syndrome, irritable bowel syndrome, and diverticulosis or after small-bowel surgery. Available in tablet and chewable forms, it should be taken with at least 8 ounces of water or juice to prevent choking and ensure its effectiveness.

LINK TO LEARNING

[Are Bulk-Forming/Fiber Supplements Safe to Take Daily? (https://openstax.org/r/mayoclinicorghli)]

Bulk-forming laxatives are often used as dietary supplements for regularity and gastrointestinal health. This Mayo Clinic post explores the benefits of taking bulk-forming laxatives daily.

Lubricant Laxatives

The goal of *lubricant laxatives* is to soften stool and lubricate the intestinal wall, making defecation easier and preventing straining. The onset of action for lubricant laxatives is typically 8–48 hours, depending on the client's normal gastrointestinal transit time. Lubricant laxatives generally do not produce increased peristatic activity that causes abdominal cramping and spasms. These laxatives are often preferred by pregnant clients and older adults. If used frequently, they may interfere with the absorption of fat-soluble vitamins (A, D, E, and K).

Mineral Oil

Mineral oil serves as a lubricant laxative for constipation or fecal impaction and facilitates the elimination of barium residue in post-GI studies. It is available in various forms, including oral liquid and rectal enema. Mineral oil is not recommended for children under age 6 or individuals with swallowing issues or incapacitation due to the risk of lipid pneumonia if aspirated. Mineral-oil enemas act fast and should be administered with care to prevent complications like bowel perforation. See Table 30.5.

Stimulant Laxatives

Stimulant laxatives intensify intestinal peristalsis and increase the volume of intestinal water to relieve acute constipation that may be caused by high-dose opioid use. Stimulant laxatives are widely used and abused by the public. Approximately 40% of chronic constipation sufferers self-medicate with laxatives (Rao & Brenner, 2021). They are commonly used as part of bowel prep before colon procedures or surgeries, but are sometimes misused to eliminate calories in an attempt to lose or maintain weight. However, such abuse can result in electrolyte imbalances, dehydration, and potential harm to the gastrointestinal system's neuromuscular functions. Stimulant laxatives may also lead to anal leakage, causing discomfort and affecting a client's confidence when leaving their home. See Table 30.5.

Bisacodyl

Bisacodyl is a stimulant laxative that directly irritates the sensory nerve endings in the smooth muscle of the intestine that induces peristalsis. Bisacodyl also stimulates an increased volume of water and electrolytes in the intestine. The action is directly responsible for the adverse effects of abdominal cramping, diarrhea, fluid, and electrolyte imbalances. Bisacodyl is typically used on a short-term basis to relieve constipation and should be taken as directed to minimize these side effects and complications.

CLINICAL TIP

Administering a Bisacodyl Suppository

- If the suppository feels soft in the foil package, return the package to the refrigerator to harden before removing the wrapper.
- Assist the client to a comfortable left side–lying position with their right knee raised to their chest.
- With a gloved hand, use a finger to insert the pointed end of the suppository about 1 inch (2.5 cm) past the rectal sphincter.

- Have the client hold the suppository in place as long as possible. Gently holding the client's buttocks together may help the client retain the suppository as long as possible, for up to 20 minutes.
- Assist the client with toileting.
- Remove gloves and wash hands thoroughly.

CLINICAL TIP

Administering a Bisacodyl Enema

- Shake the enema bottle well.
- Assist the client to a comfortable left side–lying position with their right knee raised to their chest.
- With a gloved hand, remove the protective shield and gently insert the enema tip into the rectum with the tip pointed toward the navel.
- Gently squeeze the bottle until the contents are emptied into the rectum.
- Remove the enema bottle from the rectum.
- Have the client hold the enema contents in place as long as possible, for about 10 minutes. Gently holding the client's buttocks together may help the client retain the contents.
- Assist the client with toileting.
- Remove gloves and wash hands thoroughly.

Castor Oil

Castor oil is an oral stimulant laxative used for constipation or as a bowel prep before a procedure. Castor oil is produced from the castor bean. When castor oil is in the intestine, lipase breaks down the castor oil into ricinoleic acid, a fatty acid that directly stimulates peristaltic activity of the colon to produce a bowel movement in 6–12 hours.

Castor oil is a liquid often mixed in fruit juice to mask the taste. Castor oil is contraindicated in pregnancy due to risk of inducing uterine contractions.

Senna

Senna is a laxative that converts senna glycosides to active aglycone in the colon to soften feces and stimulate peristalsis, for acute constipation and preprocedural bowel evacuation. Senna is available in tablets and as a syrup. Senna is also available in teas that are marketed for constipation relief.

Saline Laxatives

Saline laxatives are hyperosmotic oral solutions that retain water in the intestine to increase the bulk of the stool. Sometimes called "salts," these laxatives are used when there is a need for a quick emptying of the lower bowel or intestine. The salts are absorbed, causing osmotic action to draw water into the intestinal lumen of the colon and causing the fecal mass to increase in size, or "swell." The increase in bulk softens the stool for easier evacuation while also stretching the intestinal wall, causing peristaltic movement. Because the hypertonic solution offers a rapid emptying of the bowels, saline laxatives are not recommended for long-term or repeated use (Mayo Foundation for Medical Education and Research, 2023a). See Table 30.5.

Magnesium Citrate

Magnesium citrate, often referred to as *citrate of magnesia* or *mag citrate*, is a hyperosmotic saline cathartic laxative available as an oral solution. Magnesium citrate evacuates bowels before surgical or diagnostic procedures within 3–6 hours. Magnesium citrate is best given on an empty stomach with 240 milliliters (mL) of water. The solution is more palatable if chilled. Once opened, the effectiveness of magnesium citrate decreases.

Available in liquid or tablet form over the counter, magnesium citrate should be used as directed by the health care provider or per the instructions on the product label to avoid potential side effects or complications. It typically produces a bowel movement within a few hours of ingestion and is known for its effectiveness in promoting bowel regularity when needed.

Polyethylene Glycol

Polyethylene glycol is an osmotic laxative that is used for occasional and chronic constipation. This medication causes water to be drawn into the stool for easier evacuation. While it may take 2–4 days to produce results for chronic and occasional constipation, larger doses of polyethylene glycol are often used for bowel preparation before diagnostic and/or surgical procedures.

Available as a powder, a single heaping tablespoon of polyethylene glycol is reconstituted in 8 ounces of various beverages such as water, juice, soda, coffee, or tea. Stirring helps the powder dissolve, and the mixture should be consumed immediately. Typically, polyethylene glycol is taken once daily for up to 14 days, following the health care provider guidance for proper use and dosage.

Miscellaneous Laxatives

Miscellaneous laxatives are a group of drugs that do not fit into the more common categories of laxatives. These miscellaneous laxatives have different mechanisms of action and are used for the specific purpose of relieving constipation. See Table 30.5 for adult dosing of these drugs.

Linaclotide

Linaclotide is classified as an accelerant of GI transit or guanylate cyclase-C agonist. Linaclotide is used to treat irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation, to improve bowel function, to eliminate constipation, and to decrease bowel irritation. Linaclotide is contraindicated if there is a suspicion of GI obstruction. If severe diarrhea occurs, linaclotide should be stopped and the provider contacted.

Sorbitol

Sorbitol is a sugar alcohol or polyol that is commonly used as a sugar substitute in various sugar-free and "diet" food products. It is a sweet-tasting substance with approximately 60% of the sweetness of sucrose (table sugar). When taken orally, sorbitol has a laxative effect because it draws water into the intestines, softening the stool and promoting bowel movements. It is sometimes used to relieve constipation, especially in situations where a mild, osmotic laxative is needed.

Stool Softeners

Stool softeners are a type of laxative medication that helps to alleviate constipation by softening the stool, making it easier to pass. They work by increasing the water content of the stool, which helps to prevent and relieve constipation-related discomfort and straining during bowel movements. See drug emphasis Table 30.5.

Docusate Sodium and Docusate Calcium

Docusate sodium and docusate calcium are stool softeners often called surfactant laxatives. Docusate sodium and docusate calcium act like a detergent in the intestine, with anionic emulsifying and wetting properties to lower the surface tension of stool to allow penetration by water for easier defecation. Docusate sodium is available in tablets, capsules, and syrups. Docusate calcium is available as a capsule. Docusate is used prophylactically for clients at risk for constipation or fecal impaction who should avoid straining, such as postoperatively or after a myocardial infarction.

Docusate can be administered orally or rectally. Oral administration should be given with a full 8-ounce glass of water. The client should be encouraged to drink adequate fluid throughout the day. Oral solution (but not syrup) may be mixed with milk, fruit juice, or infant formula. Syrups are stored in an airtight bottle at room temperature. Rectal docusate is added to a microenema and administered via the rectum as an enema. Therapeutic effectiveness is achieved within 1–3 days.

Table 30.5 lists common laxatives and stool softeners with typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Bulk-Forming Laxatives	
Psyllium (Fiberall, Konysl)	*Oral (powder):* 1 rounded tbsp (12 g) 3 times daily. *Oral (granules):* 1 tsp (6 g) 1–3 times daily. *Oral (0.52 g capsule):* 5 capsules with at least 8 oz of liquid, up to 3 times daily.

TABLE 30.5 **Drug Emphasis Table: Laxatives and Stool Softeners** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Methycellulose (Citrucil)	*Oral:* Start with two 500 mg caplets, increased as needed up to 6 times daily. Do not exceed 12 caplets per day.
Calcium polycarbophil (FiberCon)	*Oral:* Two 625 mg tablets 1–4 times per day.
Lubricant Laxatives	
Mineral Oil	*Oral (liquid):* 1–2 tbsp at bedtime. *Rectal (enema):* 1 bottle (120 mL) daily.
Stimulant Laxatives	
Bisacodyl Pr (Dulcolax, Correctol)	*Oral (5 mg tablet):* 1–3 tablets in a single dose daily. *Rectal (suppository):* 10 mg (1 suppository) once daily.
Castor oil (Emulsoil)	*Oral (liquid):* 15–60 mL in a single daily dose.
Senna (Senokot)	*Oral (tablet):* 1 tablet once or twice daily. *Oral (liquid):* 10–30 mL up to 2 times daily.
Saline Laxatives	
Magnesium citrate (Citroma)	*Oral (liquid):* 6.5–10 fl. oz. daily. Maximum dose: 10 fl. oz. in 24 hours.
Polyethylene glycol (Miralax)	*Oral (powder):* 17 g of powder dissolved in 4–8 oz of beverage daily. Do not use for more than 7 days.
Miscellaneous Laxatives	
Linaclotide (Linzess)	*For IBS with constipation, oral:* 290 mcg tablet once daily. *For chronic idiopathic constipation, oral:* 145 mcg tablet once daily.
Sorbitol (Arlex)	*Rectal (enema):* 120 mL daily as needed.
Stool Softeners	
Docusate sodium (Colace)	*Oral:* 1–3 100 mg softgels daily.
Docusate calcium (Surfak)	*Oral:* 240 mg softgel once daily for 2–3 days or until bowel movements are normal.

TABLE 30.5 **Drug Emphasis Table: Laxatives and Stool Softeners** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Typical adverse effects of laxatives and stool softeners include abdominal cramping, diarrhea, electrolyte imbalances (particularly sodium and potassium), dehydration, rectal irritation, and gas and bloating.

Contraindications for laxatives and stool softeners include hypersentivitity to the drug or any of its components, intestinal blockage, appendicitis, and certain medical conditions such as Crohn's disease or ulcerative colitis.

Laxatives should be used cautiously, as over time the body can become reliant on the drug to have bowel movements, leading to a condition known as laxative dependency. This can make it harder to have regular bowel movements without the use of laxatives.

Table 30.6 is a drug prototype table for laxatives and stool softeners featuring psyllium. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Bulk-forming laxative **Mechanism of Action** Adds bulk to stool through water absorption, which promotes peristalsis and natural elimination	**Drug Dosage** *Oral (powder):* 1 rounded tbsp (12 g) 3 times daily. *Oral (granules):* 1 tsp (6 g) 1–3 times daily. *Oral (0.52 g capsule):* 5 capsules with at least 8 oz of liquid, up to 3 times daily.
Indications Short-term relief of occasional constipation and to promote regularity **Therapeutic Effects** Bowel movement within 12–72 hours	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Abdominal cramping Diarrhea Electrolyte imbalances Rectal irritation Gas/bloating	**Contraindications** Hypersensitivity to the drug or any of its components Caution: Taking this product without adequate fluid may cause it to swell and block the throat or esophagus, causing choking; should not be taken if difficulty swallowing is present

TABLE 30.6 **Drug Prototype Table: Psyllium** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking laxatives or stool softeners:

- Prior to administering, assess the client's medical history, current drug list, and allergies.
- Educate the client regarding laxative and stool effects, such as abdominal cramping, diarrhea, and rectal irriation.
- Assess client's bowel habits including frequency, consistency, and ease of bowel movements. Monitor for changes with laxative and stool softener administration.
- Monitor electrolyte levels, particularly sodium and potassium, to detect abnormalities.
- Educate the client on lifestyle and dietary factors, such as increasing hydration and eating a healthy diet high in fiber to prevent constipation.
- Educate client that these drugs are for short-term use, and long-term use could result in dependence.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLINICAL TIP

Fecal Impaction and Bowel Obstruction

When administering laxatives and stool softeners, the nurse should assess the client for signs and symptoms of fecal impaction and bowel obstruction, which include severe abdominal bloating and cramping, stool leakage or sudden watery diarrhea (around impaction), rectal bleeding, small semi-formed stools, severe abdominal pain, vomiting, loud sounds from the abdomen, and inability to pass flatulence.

CLIENT TEACHING GUIDELINES

The client taking a laxative or a stool softener should:

- Increase their dietary intake of fiber and increase their fluid intake, if not contraindicated, to help reduce the risk of constipation.
- Report signs of muscle weakness, muscle cramps, fatigue, retrosternal pain, or numbness or tingling in the

arms, legs and face, as these may be symptoms of serious adverse effects of the drugs.

The client taking a laxative or a stool softener *should not:*

- Take these drugs long term, as they may result in dependence.

FDA BLACK BOX WARNING

Linaclotide

Linaclotide is contraindicated in clients less than 2 years of age as it as been shown to cause death secondary to severe dehydration.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Mae Belle Smith is a 24-year-old logistics manager. Her job requires long hours of sitting at a desk with few breaks for hydration. Mae Belle presented to her provider with complaints of severe abdominal pain and distention and has not had a bowel movement in 6 days other than occasional leakage of scant amounts of liquid stool. Current medications include over-the-counter ibuprofen for occasional headaches.

Vital Signs		Physical Examination
Temperature:	99.5°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; S1, S2 noted • *Respiratory:* Clear to auscultation bilateral all lung fields • *GI:* Abdomen distended, lower abdomen firm, hypoactive bowel sounds in all 4 quadrants • *Neurological:* Within normal limits • *Integumentary:* No wounds noted; skin appropriate for age.
Blood pressure:	122/68 mm Hg	
Heart rate:	93 beats/min	
Respiratory rate:	20 breaths/min	
Oxygen saturation:	99% on room air	
Height:	5'7"	
Weight:	125 lb	

TABLE 30.7

1. The health care provider suspects Mae Belle has a fecal impaction. Which of the following medications should the nurse anticipate will be ordered?
   a. Methylcellulose
   b. Sorbitol
   c. Mineral oil
   d. Docusate sodium

2. After the impaction is resolved, which of the following medications should the nurse anticipate the health care provider will order to help promote the client's natural bowel function?
   a. Psyllium
   b. Loperamide
   c. Linaclotide
   d. Ondansetron

Chapter Summary

This chapter discussed gastrointestinal disturbances such as nausea, vomiting, motion sickness, constipation, and diarrhea, which are often symptoms of an underlying condition. While treatment of the GI symptom is a priority, providers should explore the potential causes of the symptoms. Antiemetics, antidiarrheals, and laxatives may only be temporary solutions until the primary cause is discovered and treated.

The text also noted that the GI system is vulnerable to fluid and electrolyte imbalances from GI disturbances as well as GI medications. Nurses must consistently assess GI status, the risk of dehydration, and electrolyte imbalances. Nurses should encourage clients to drink at least 2 liters of water a day, unless contraindicated, to promote a healthy GI tract and to optimize its proper functioning.

Key Terms

anticholinergic effects common effects such as dry mouth, dry eyes, blurred vision, urinary retention, constipation, and cognitive dysfunction resulting from the blockade of cholinergic receptors

antidiarrheals medications used to treat and manage diarrhea

antiemetics medications that prevent or treat nausea and vomiting

chemoreceptor trigger zone (CTZ) an area of neural receptors on the floor of the fourth ventricle of the brain within the dorsal surface of the medulla oblongata that communicates with the vomiting center for emesis

extrapyramidal symptoms dysfunctional involuntary movements such as akathisia (restlessness and/or tapping or jiggling of fingers or legs), dystonia (painful involuntary muscle contractions), Parkinsonism (symptoms similar to Parkinson's disease such as tremors, difficulty thinking and/or speaking, or stiff facial muscles), and tardive dyskinesia (involuntary facial movements such as eye blinking, sticking out tongue, and/or chewing or sucking motion)

laxatives medications used to treat constipation

phenothiazines a group of medications with antagonistic dopamine used as an antipsychotic or antiemetic

stool softeners medications used to soften stools and ease defecation

vomiting center an area in the central medulla of the brain innervating the vagus nerve and spinal motor neurons in conjunction with the CTZ to cause vomiting

Review Questions

1. A nurse is instructing a client being discharged with a prescription for diphenoxylate with atropine. Which of the following instructions should be given to the client?
   a. It will take 2 weeks before the full effects of the medication are achieved.
   b. Take the prescribed amount of medication every day, even if your symptoms improve.
   c. Keep some throat lozenges handy as dry mouth is a common side effect of this medication.
   d. This medication will not make you drowsy.

2. A nurse is preparing to administer a bisacodyl suppository to a client. Which of the following interventions is appropriate to ensure safe and effective administration?
   a. Have the client lie on their right side with their left knee raised to their chest.
   b. Have the client lie on their left side with their right knee raised to their chest.
   c. Remove the suppository from the refrigerator at least 15 minutes before administration to allow it to soften.
   d. Instruct the client to stand and get dressed immediately after administration.

3. The nurse is assessing a client with a new prescription for chlorpromazine. The nurse recognizes the client is having an adverse effect when the client complains of:
   a. Dry mouth
   b. Flu-like symptoms
   c. Increased urination
   d. Diarrhea

4. A client is admitted to the hospital with Stage III chronic kidney disease and constipation. Which of the following laxatives is contraindicated for this client?
    a. Magnesium citrate
    b. Bisacodyl
    c. Psyllium
    d. Polyethylene glycol

5. An ED nurse is triaging a client who was recently started on ondansetron for chemotherapy-induced nausea and vomiting (CINV). The nurse recognizes the following symptom as a side effect of ondansetron:
    a. Photosensitivity
    b. Increased urination
    c. Peripheral edema
    d. Headache

6. The nurse is discharging a client home with a new prescription for docusate sodium. What information should the nurse include in discharge teaching?
    a. This medication must be taken at bedtime.
    b. Take the medication with a full glass of water.
    c. This medication must be taken long term for it to be fully effective.
    d. Take the medication on an empty stomach.

7. When assessing a client who has just started taking loperamide after experiencing diarrhea for a week, which of the following findings would be most concerning?
    a. Nausea
    b. Decreased appetite
    c. Changes in stool consistency
    d. Decreased blood pressure

8. The nurse is administering linaclotide for a client. For which of the following conditions is this laxative contraindicated?
    a. Bowel obstruction
    b. Irritable bowel syndrome
    c. Chronic idiopathic constipation
    d. Bowel irritation

9. The nurse is treating a client with nausea, vomiting, and dizziness secondary to inner-ear problems. Which of the following medications should the nurse anticipate will be prescribed?
    a. Ondansetron
    b. Aprepitant
    c. Meclizine
    d. Prochlorperazine

10. The nurse is teaching a client how to use a scopolamine patch. Which of the following statements by the client indicates the need for further instruction?
    a. “I need to put this on as soon as I start to feel nauseated.”
    b. “One patch should last 3 days.”
    c. “I need to wash my hands after applying the patch.”
    d. “I should not touch the adhesive section when applying the patch.”

CHAPTER 31
Hyperacidity and Antiulcer Drugs

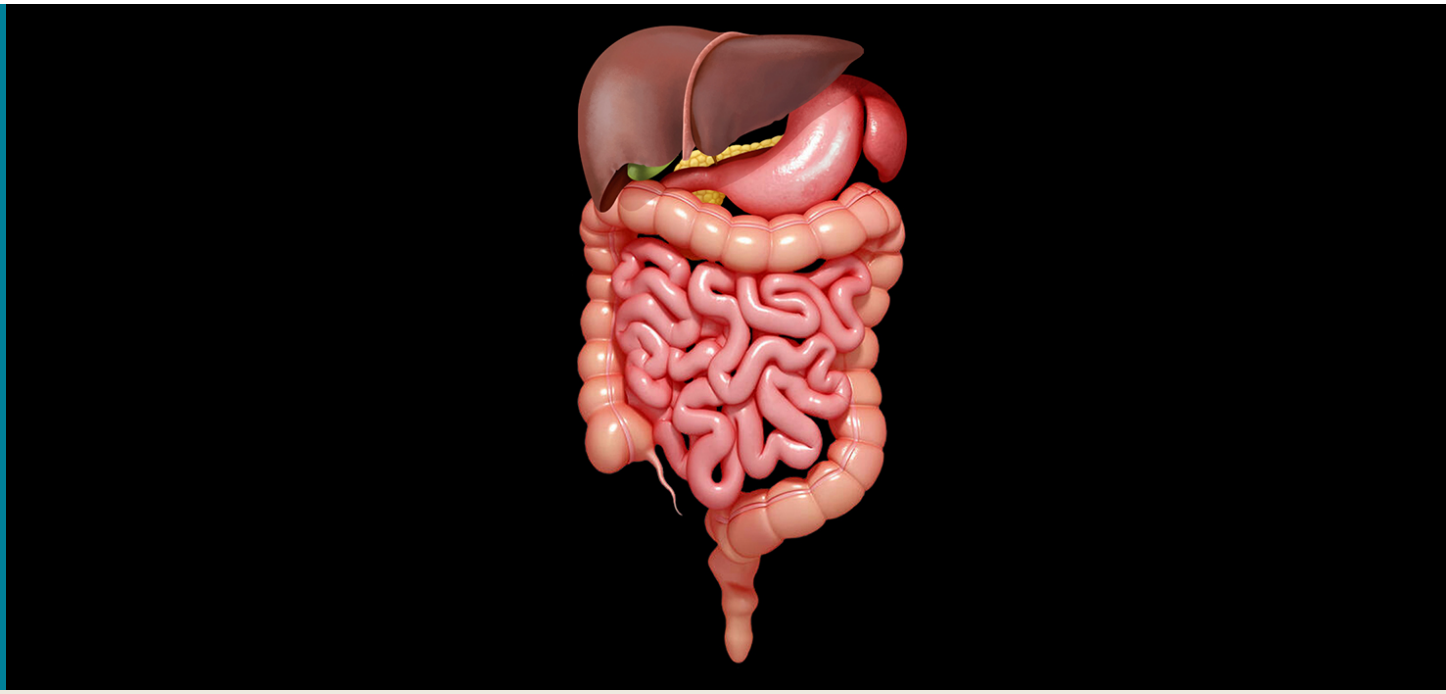


FIGURE 31.1 The digestive system breaks down food into nutrients that can be absorbed into the bloodstream to give the body energy and the ability to grow and repair itself. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION **Hyperacidity** is a condition in which the stomach produces an excessive amount of stomach acid, primarily **hydrochloric (HCl) acid**. This excess acid production can lead to various gastrointestinal symptoms, including heartburn, regurgitation, abdominal discomfort, and in severe cases can contribute to the development of conditions such as **gastroesophageal reflux disease (GERD)** and **peptic ulcer disease (PUD)**.

Hyperacidity can result from factors such as dietary choices, lifestyle habits, certain medications, or underlying medical conditions. This chapter will review drugs used to treat and manage hyperacidity disorders, including GERD and PUD.

31.1 Antacids

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 31.1.1 Identify the characteristics of antacid drugs used to treat GI disorders.
- 31.1.2 Explain the indications, action, adverse reactions, and interactions of antacid drugs used to treat GI disorders.
- 31.1.3 Describe nursing implications of antacid drugs used to treat GI disorders.
- 31.1.4 Explain the client education related to antacid drugs used to treat GI disorders.

Antacids are a class of over-the-counter medications that are used to neutralize or reduce gastric hyperacidity. **Antacids** are also beneficial in treating duodenal and gastric ulcers, gastritis, pancreatic insufficiency, biliary reflux, and phosphate binding in chronic renal failure. The goals of antacid therapy are to alleviate symptoms of heartburn

and indigestion such as pain, as well as stomach spasms. Antacids are recommended for short-term use only.

A combination of antacid ingredients is most often used to balance the therapeutic effects and avoid adverse effects. Various salts of calcium, aluminum, and magnesium neutralize gastric acids (Salisbury & Terrell, 2022). Antacids are available in many forms, including tablets, chewable tablets, liquid suspensions, and effervescent powders.

Sodium Bicarbonate

Sodium bicarbonate is an alkaline substance that neutralizes excess stomach acid. When sodium bicarbonate comes in contact with stomach acid, it reacts with the acid to form water, carbon dioxide, and sodium chloride, also known as common table salt. It is commonly used orally as a tablet or powder to alleviate the burning sensation and discomfort caused by indigestion or heartburn. Because it contains sodium, it may not be suitable for individuals on sodium-restricted diets or those with conditions that cause fluid retention, such as heart failure and chronic kidney disease. See drug emphasis Table 31.1 for dosing information.

Calcium Carbonate

Calcium carbonate is a fast-acting oral antacid that efficiently neutralizes gastric acids, offering relief from heartburn and associated symptoms. It also serves as a calcium supplement, beneficial for conditions such as osteoporosis and hypocalcemia. Calcium carbonate also aids peristalsis in the esophagus, reducing acid reflux by pushing gastric acid back into the stomach (Salisbury & Terrell, 2022). It effectively treats hyperacidity symptoms linked to various conditions, including indigestion, esophagitis, and hiatal hernia. In clients with chronic renal failure and hyperphosphatemia, calcium carbonate helps manage excess phosphorus due to kidney insufficiency.

Calcium carbonate is administered by mouth as a sustained-released capsule, chewable tablet, or a powder that can be mixed in water. Chewable tablets must be chewed thoroughly before swallowing. Sustained-released capsules should be swallowed whole and never chewed. When taken as an antacid, calcium carbonate is administered 1 hour after meals and at bedtime. Calcium supplements should always be taken with vitamin D, as vitamin D is essential for efficient absorption of calcium (Rosen, 2023). See drug prototype Table 31.2 for additional information.

Aluminum Hydroxide

Aluminum hydroxide is a formulation of aluminum hydrochloride and water. It functions as an antacid by neutralizing excess stomach acid, primarily hydrochloric acid. It raises the pH (a measure of acidity) of gastric and esophageal secretions to reduce acid by making the secretions more alkaline.

Aluminum hydroxide is used to relieve intermittent hyperacidity symptoms from gastritis, GERD, and hiatal hernia. It may also be used as an adjunct medication for ulcers (gastric and duodenal) due to its alkalization properties. It is often used in combination with other antacids. These combination antacids provide both acid-neutralizing properties and relief from potential constipation. See drug emphasis Table 31.1 for dosing information.

Magnesium Hydroxide

Magnesium hydroxide is a commonly used active ingredient in antacid medications. Its role involves the neutralization of stomach acid. Similar to the other antacids mentioned in this chapter, it achieves this by leveraging its alkaline properties to counteract excessive stomach acidity. Magnesium hydroxide is often combined with aluminum hydroxide, and sometimes simethicone, to provide relief from heartburn, indigestion, and upset stomach with gas and bloating.

Magnesium hydroxide also has a laxative effect by causing osmotic fluid retention in the colon. This results in colon distention that stimulates peristalsis. When taken in larger quantities or more frequently than recommended, magnesium hydroxide can act as a mild laxative, potentially resulting in diarrhea. The magnesium in magnesium hydroxide can impact phosphorous digestion. Magnesium and phosphorus engage in a competitive absorption process within the small intestine. When there is a substantial disparity in the dietary intake of these minerals, one may hinder the absorption of the other, potentially leading to a deficiency in the inhibited mineral.

Magnesium hydroxide is an aqueous suspension that needs to be shaken well before use to mix the suspension.

Magnesium hydroxide is most effective when administered on an empty stomach. It is best administered in the morning or at bedtime. Doses should be followed by at least 8 ounces of water if used as a laxative. The medication should be stored at 15°–30°C (59°–86°F). See drug emphasis Table 31.1 for dosing information.

Table 31.1 lists the common antacids and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Sodium bicarbonate (Alka-Seltzer)	2–4 tablets orally every 4 hours. Maximum dose: 24 tablets in 24 hours. ½ level tsp in 4 oz of water every 2 hours. Maximum dose: 3 tsp. in 24-hour period.
Calcium carbonate (Tums, Rolaids)	1–4 (10 gr/648 mg) tablets orally daily. Maximum dose: 4 tablets in 24 hours. 2–4 (500 mg) chewable tablets orally when symptoms occur. Maximum dose: 8 tablets in 24 hours. May decrease absorption of all medications; recommend taking 1 hour before or 2 hours after other medications.
Aluminum hydroxide (Amphojel)	10 mL 5–6 times orally daily after meals and at bedtime followed by a sip of water. Maximum dose: 60 mL in 24 hours.
Magnesium hydroxide (Milk of Magnesia)	5–15 mL with water orally up to 4 times daily.

TABLE 31.1 Drug Emphasis Table: Antacids (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Typical adverse effects of antacids include constipation (particularly those containing aluminum or calcium when used in large amounts or for extended periods of time), diarrhea (specifically antacids containing magnesium, which have a laxative effect), **rebound hyperacidity** (when the antacid wears off and the stomach produces additional acid), kidney stones (particularly from antacids containing calcium, as some kidney stones are caused by calcium oxalate), and gas and bloating.

When used excessively or for prolonged periods of time, antacids can potentially lead to electrolyte imbalances. The specific electrolyte imbalance that can result from antacid use depends on the types of minerals they contain. Electrolyte imbalances associated with antacids include:

- *Hypercalcemia:* Antacids that contain calcium, such as calcium carbonate, can lead to elevated calcium levels in the bloodstream. Symptoms may include excessive thirst, frequent urination, abdominal pain, nausea, vomiting, constipation, and fatigue.
- *Hypermagnesemia:* Antacids containing magnesium, like magnesium hydroxide, can cause elevated magnesium levels. Symptoms may include muscle weakness, nausea, vomiting, diarrhea, low blood pressure, and in severe cases, cardiac arrhythmias and respiratory distress.
- *Hypernatremia:* Antacids containing sodium, like sodium bicarbonate, can cause elevated sodium levels. Symptoms may include excessive thirst, dry mouth, confusion, restlessness, edema, or muscle twitching.
- *Hypophosphatemia:* Although less common, antacids (particularly magnesium hydroxide) can potentially interfere with the absorption of phosphate in the digestive tract, leading to low phosphorous levels in the blood. Symptoms may include muscle weakness, bone pain, confusion, and fatigue.

Contraindications to antacids include hypersensitivity to the antacid or any of its components. Individuals with kidney disease or heart failure should use antacids containing magnesium, aluminum, or sodium cautiously, as these may impact kidney function.

Table 31.2 is a drug prototype table for antacids featuring calcium carbonate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and

contraindications.

Drug Class Antacid **Mechanism of Action** Decreases gastric acidity and inhibits proteolytic action of pepsin on gastric mucosa	**Drug Dosage** 1–4 (10 gr/648 mg) tablets orally daily. Maximum dose: 4 tablets in 24 hours. 2–4 (500 mg) chewable tablets orally when symptoms occur. Maximum dose: 8 tablets in 24 hours. May decrease absorption of all medications; recommend taking 1 hour before or 2 hours after other medications.
Indications To manage GI hyperacidity conditions such as heartburn, acid indigestion, sour stomach, upset stomach **Therapeutic Effects** Relieves acid indigestion, heartburn, and sour stomach	**Drug Interactions** Digoxin Magnesium-containing agents Tetracyclines Fluroquinolones **Food Interactions** No significant interactions
Adverse Effects Constipation Flatulence	**Contraindications** Hypersensitivity

TABLE 31.2 **Drug Prototype Table: Calcium Carbonate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antacids:

- Prior to administering, assess the client's medical history, current drug list, and allergies.
- Educate the client regarding antacid effects, such as constipation, gas, and diarrhea.
- Monitor fluid intake and urine output (I&Os) for urinary retention and edema with sodium bicarbonate.
- Provide the client with teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antacid should:

- Chew oral tablets thoroughly before swallowing.
- Drink 8 ounces of fluid after taking antacids.
- Shake suspensions well to adequately mix the ingredients before taking.
- Take 1 hour before or 2 hours after other medications.
- Reports effects such as muscle twitching, **tetany**, edema, or bone pain to the health care provider as these may be symptoms of a severe adverse reaction.

The client taking an antacid *should not:*

- Take two different types of antacids at the same time.
- Use for more than 2 weeks.

31.2 Histamine Blockers and Proton-Pump Inhibitors

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 31.2.1 Identify the characteristics of histamine-blocker and proton-pump inhibitor drugs used to treat GI disorders.
- 31.2.2 Explain the indications, action, adverse reactions, and interactions of histamine-blocker and proton-pump inhibitor drugs used to treat GI disorders.
- 31.2.3 Describe nursing implications of histamine-blocker and proton-pump inhibitor drugs used to treat GI disorders.
- 31.2.4 Explain the client education related to histamine-blocker and proton-pump inhibitor drugs used to treat GI disorders.

Histamine blockers, known as H2 blockers, and proton-pump inhibitors (PPIs) belong to the categories of drugs used to mitigate or hinder the production of stomach acid. These medications find widespread application in the treatment of conditions associated with heightened gastric acid secretion, encompassing gastroesophageal reflux disease (GERD), peptic ulcers, and heartburn.

Histamine Blockers

Histamine blockers, also called histamine H2-receptor antagonists or H2 blockers, have GI antisecretory action. By blocking the H2 receptors, drugs in this classification suppress gastric acid secretions and lower the hydrogen ion concentration of the gastric contents by attaching to the histamine (H2) receptor sites on gastric cells. Therefore, they prevent or treat heartburn, acid indigestion, gastric and duodenal ulcers, GERD, and hypersecretory conditions such as **Zollinger-Ellison syndrome**. H2 blockers are often used concurrently with antibiotics to treat *H. pylori*-associated peptic ulcer disease (PUD).

LINK TO LEARNING

Antisecretory Drug Therapy (https://openstax.org/r/zollinger)

This article from the Mayo Clinic helps with understanding antisecretory drug therapy and how it is beneficial in hypersecretory conditions such as Zollinger-Ellison syndrome.

Cimetidine

Cimetidine is an antisecretory medication used for short-term treatment of heartburn, erosive GERD, and gastric or duodenal ulcers. Prophylactic use of cimetidine includes prevention of stress ulcers or management of hypersecretory conditions such as Zollinger-Ellison syndrome. Cimetidine has a high selectivity for the H2 receptors on the parietal cells of the stomach. (Pino & Azer, 2023) Occupying these receptor sites inhibits all phases of basal (daytime and nocturnal) gastric acid secretion. By blocking the parietal cells, gastric acid production is reduced, raising the pH of gastric contents. This results in an indirect reduction of **pepsin** secretion. See drug prototype Table 31.4 for additional drug information.

Famotidine

Famotidine, a histamine inhibitor, is commonly used to treat heartburn, GERD, PUD, and hypersecretory conditions. Famotidine reduces the output of hydrochloric acid from the parietal cells, which in turn reduces the erosive damage to the gastric mucosa that may occur from hyperacidity. Famotidine is an effective prophylactic drug for stress ulcers and perioperative aspiration pneumonia. It is available orally and intravenously. See drug emphasis Table 31.3 for dosing information.

Nizatidine

Nizatidine blocks histamine at the H2 receptors of the parietal cells, significantly reducing the secretion of nocturnal gastric acid for up to 12 hours. It is an effective drug for GERD, gastric ulcers, and duodenal ulcers. Nizatidine may also be used for prevention of stress ulcers or the abolition of *H. pylori.* The medication is generally given twice per day for up to 8 weeks. If nizatidine is ordered daily, it is generally given at bedtime. See drug emphasis Table 31.3 for dosing information.

Table 31.3 lists common histamine blockers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Cimetidine (Tagamet HB)	*For GERD:* 400 mg orally 4 times daily or 800 mg orally twice daily for up to 12 weeks. *For heartburn/dyspepsia:* 200 mg orally 2–4 times daily. Reduce daily dosage by 50% if the client's CrCl (creatinine clearance) is less than 30 mL/hour. Intermittent intravenous infusion: 300 mg every 6–8 hours infused over 15–20 minutes. Continuous intravenous infusion: 37.5 mg/hour (900 mg/day).
Famotidine (Pepcid)	*For GERD/gastritis:* 20 mg orally twice daily for up to 8 weeks. *For heartburn/dyspepsia:* 20 mg orally 10–60 minutes before meals. *For hypersecretory conditions:* 20 mg orally every 6 hours or 20 mg intravenously every 12 hours.
Nizatidine (Axid)	*For GERD/gastritis:* 150 mg orally twice daily for up to 12 weeks. *For gastric/duodenal ulcers:* 150 mg orally twice daily or 300 mg orally at bedtime for up to 8 weeks.

TABLE 31.3 Drug Emphasis Table: Histamine Blockers (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Typical adverse effects of histamine blockers include diarrhea, headaches, mental confusion, agitation, depression, **gynecomastia**, **neutropenia**, **agranulocytosis**, increases in serum **transaminase**, **arthralgia**, rash, and **alopecia**. In rare cases, bradycardia, tachycardia, and AV heart block have been reported. Contraindications include hypersensitivity to the drug or any of its components.

Table 31.4 is a drug prototype table for histamine blockers featuring cimetidine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class H2-receptor antagonists/blockers **Mechanism of Action** Blocks H2 receptors, thereby suppressing gastric acid secretion, and lowers the hydrogen ion concentration in the stomach	**Drug Dosage** *For GERD:* 400 mg orally 4 times daily or 800 mg orally twice daily for up to 12 weeks. *For heartburn/dyspepsia:* 200 mg orally 2–4 times daily. Reduce daily dosage by 50% if the client's CrCl is less than 30 mL/hour. *Intermittent intravenous infusion:* 300 mg every 6–8 hours infused over 15–20 minutes. *Continuous intravenous infusion:* 37.5 mg/hour (900 mg/day).
Indications Short-term treatment of active duodenal and active benign gastric ulcers, erosive GERD, and hypersecretory conditions **Therapeutic Effects** Decreases gastric acids to provide symptomatic relief of hyperacidic GI conditions	**Drug Interactions** Warfarin Phenytoin Theophylline Metronidazole Ketoconazole **Food Interactions** No significant interactions
Adverse Effects Diarrhea Headaches Dizziness Confusion Agranulocytosis Gynecomastia	**Contraindications** Hypersensitivity Caution: Rare instances of cardiac arrhythmias and hypotension have been reported following the rapid administration of cimetidine hydrochloride injection by intravenous bolus

TABLE 31.4 **Drug Prototype Table: Cimetidine** (source: https://dailymed.nlm.nih.gov/dailymed/)

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Logan Gomez is a 35-year-old parent of two presenting to the health care provider with reports of burning in the upper part of the abdomen. The pain develops after eating. Often the pain wakes them from sleeping. Logan schedules an appointment with the provider.

Vital Signs		Physical Examination
Temperature:	98.4° F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* Within normal limits • *Respiratory:* Within normal limits • *GI:* Abdomen soft, nontender, distended with hyperactive BS in all four quadrants • *GU:* Reports normal urine output • *Neurological:* Within normal limits • *Integumentary:* No wounds noted; skin appropriate for age
Blood pressure:	118/66 mm Hg	
Heart rate:	88 beats/min	
Respiratory rate:	16 breaths/min	
Oxygen saturation:	97% on room air	
Height:	5'8"	
Weight:	145 lb	

TABLE 31.5

1. The client is diagnosed with peptic ulcer disease. Which medication does the nurse anticipate the provider will order for Logan?
   a. Sodium bicarbonate
   b. Amphojel
   c. Milk of Magnesia
   d. Famotidine

2. The nurse is educating the client on the newly prescribed medication. Which of the following statements by the client indicates understanding?
   a. "I should stop taking the medication immediately when I feel better."
   b. "While I am taking this medication I will avoid alcohol, spicy foods, and ibuprofen."
   c. "It may help to take my antacid with the medication."
   d. "This medication will give me extra energy."

Proton Pump Inhibitors

Proton pump inhibitors (PPIs) are antisecretory drugs that block both basal and stimulated gastric acid production. Gastric acid secretions are reduced by irreversibly blocking gastric hydrogen and potassium ATPase, an enzyme that produces gastric acid. Short-term use of PPIs for 4–6 weeks is an effective treatment for gastric and duodenal ulcers, GERD, and erosive esophagitis. The long-term use of PPIs is useful in hypersecretory conditions such as Zollinger-Ellison syndrome. Prophylactic use of PPIs is administered for clients at risk for stress ulcers, such as trauma clients on mechanical ventilation.

Omeprazole

Omeprazole is the prototype antisecretory PPI that suppresses the secretion of gastric acid by inhibiting the gastric proton pump found within the parietal cells. Various chemicals such as acetylcholine, histamine, and gastrin bind to receptors on parietal cells, prompting activation of hydrogen (H^+), potassium (K^+), and ATPase enzymes (the proton pump) that produces gastric acid secretion. Suppressing this action relieves GI distress to allow for healing of the mucosal lining.

Omeprazole is commonly used for dyspepsia (occurring at least twice per week), GERD, duodenal and gastric ulcers, erosive esophagitis, and prophylactically to prevent gastric ulcers related to the use of nonsteroidal antiinflammatory drugs (NSAIDs). Typical treatment is 4–8 weeks, along with diet and lifestyle modifications. Short-

term use in combination with clarithromycin may be used to treat duodenal ulcers associated with *H. pylori* infections.

Omeprazole is available for oral use as a capsule, delayed-release tablet, and powder for oral suspension. Oral capsules and delayed-released tablets are best administered 30–60 minutes before breakfast. These must be swallowed whole and should not be opened, chewed, or crushed. It may take several days for omeprazole to take effect. In these cases, occasionally omeprazole is administered along with antacids until the omeprazole takes effect. Oral-suspension omeprazole may be administered via a gastrostomy tube. The omeprazole suspension contains granules that must be diluted in water. See drug prototype Table 31.7 for additional information.

Pantoprazole

Pantoprazole is a PPI used short-term for GERD and to manage or prevent erosive esophagitis. It is also useful in managing hypersecretory diseases, peptic ulcer disease, duodenal ulcers, dyspepsia, heartburn, and for stress ulcer prophylaxis. Pantoprazole suppresses gastric acid production by inhibiting the proton pump in the parietal cells.

Pantoprazole is available in delayed-release tablets, granules to create an oral suspension, and as a reconstituted solution for parenteral use. Tablets should be taken whole with or without food, without chewing, crushing, or breaking them. Granules may be administered orally or via a gastric tube. Oral suspension and granules may only be administered in apple juice or applesauce; the medication should not be mixed with water or other liquids or foods (Pfizer, 2023). However, the nurse should recommend that clients take small sips of water after administration to ensure the granules are washed down into the stomach. Pantoprazole is typically not used for longer than 8 weeks, especially in older clients. See drug emphasis Table 31.6 for dosing.

Esomeprazole

Esomeprazole is a weak base isomer of omeprazole that is converted to its active form in a highly acidic gastric environment. It inhibits the proton pump in parietal cells, significantly decreasing basal and stimulated gastric acid secretions.

Esomeprazole is an effective PPI that supports healing of erosive esophagitis, treatment of heartburn, prevention of recurrent gastric or duodenal ulcers, and ulcer prophylaxis with NSAID use. Additionally, esomeprazole is effective in the management of GERD, ulcers, and hypersecretory disease such as Zollinger-Ellison syndrome.

Esomeprazole is available in capsules, oral suspension, and powder for reconstitution for injection. The drug is destroyed in acidic environments; therefore, esomeprazole capsules are produced to allow for delayed absorption in the small intestine. Capsules must be swallowed whole and cannot be crushed or chewed. If a client cannot swallow capsules, the capsule may be opened and the capsule pellets mixed in applesauce The nurse should emphasize that the applesauce, once mixed, must be swallowed promptly without chewing the pellets to ensure the medication remains effective. Direct parenteral administration of esomeprazole must be reconstituted. See drug emphasis Table 31.6 for dosing.

Lansoprazole

Lansoprazole is a PPI that suppresses gastric acid formation, making it effective for short-term use to treat duodenal ulcers, erosive esophagitis, and GERD and as maintenance treatment for hypersecretory disorders. Lansoprazole is rapidly absorbed from the GI tract after leaving the stomach. The onset to reduce acid is approximately 2 hours. Ulcer symptom relief is generally acquired within the first week of its use. Lansoprazole is available as a sustained-release capsule and oral disintegrating tablets. See drug emphasis Table 31.6 for dosing.

Table 31.6 lists common PPIs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Omeprazole (Prilosec)	20 mg (delayed-release or disintegrating tablet) orally once daily for 14 days.
Pantoprazole (Protonix)	40 mg orally once daily for 4–8 weeks or 40 mg intravenously once daily for 7–10 days.

TABLE 31.6 Drug Emphasis Table: PPIs (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Esomeprazole (Nexium)	20 mg orally or 20–40 mg intravenously once daily for 4–8 weeks.
Lansoprazole (Prevacid)	15 mg orally once daily 30 minutes before a meal for 14 days.

TABLE 31.6 **Drug Emphasis Table: PPIs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Typical adverse effects include headache, dizziness, nausea, vomiting, abdominal pain, diarrhea, and cough. Contraindications of PPIs include hypersensitivity to PPIs and the drug rilpivirine, an HIV medication.

Table 31.7 is a drug prototype table for PPIs featuring omeprazole. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Proton pump inhibitor (PPI); antisecretory **Mechanism of Action** Suppresses gastric acid secretion by inhibiting the H^+, K^+, ATPase enzyme system (proton pump)	**Drug Dosage** 20 mg (delayed-release or disintegrating tablet) orally once daily for 14 days.
Indications Short-term treatment of peptic ulcer, duodenal, and gastric ulcer diseases *H. pylori* infection GERD Erosive esophagitis Hypersecretion conditions Uncomplicated heartburn **Therapeutic Effects** An antiulcer agent that suppresses gastric acid secretion to relieve and promote ulcer healing	**Drug Interactions** Amoxicillin Clarithromycin Diazepam Proguanil Moclobemide Phenytoin Warfarin **Food Interactions** No significant food interactions
Adverse Effects Diarrhea Abdominal pain Headache Nausea/vomiting Cough Back pain Dizziness	**Contraindications** Hypersensitivity Rilpivirine

TABLE 31.7 **Drug Prototype Table: Omeprazole** (source: https://dailymed.nlm.nih.gov/dailymed/; Shah & Gossman, 2023)

CLINICAL TIP

Assess for Worsening GI Symptoms

When assessing a client's response to medications for hyperacidity and antiulcer treatment, monitor signs and symptoms of GI distress—weight, bowel habits, nausea, vomiting, abdominal pain, bloating, or belching. Follow provider instruction on dietary intake; some GI conditions require increased fiber and fluids, while others may require "bowel rest" that involves smaller meals with soft foods.

Nursing Implications

The nurse should do the following for clients who are taking histamine blockers and proton pump inhibitors:

- Prior to administering, assess the client's medical history, current drug list, and allergies.
- Educate the client regarding duration of use for these medications being short term, typically 4–8 weeks.
- Teach the client to avoid trigger foods that increase stomach acidity such as spicy foods, fried foods, and caffeine.
- Monitor for respiratory infection and/or pneumonia with PPI administration as these may lead to an overgrowth of bacteria in the upper GI tract that can migrate to the lungs.
- Provide the client with teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a histamine blocker and proton pump inhibitor should:

- Adhere to dosing regimen as prescribed by the health care provider, typically short-term administration of 4–8 weeks.
- Avoid trigger foods such as fast food, fried foods, spicy foods, caffeine, tea, and colas as these may increase stomach acid.
- Reports effects such as cough, fever, and shortness of breath to the health care provider as these may be symptoms of a severe adverse reaction.

The client taking a histamine blocker and proton pump inhibitor *should not:*

- Use for longer than prescribed.

31.3 Pepsin Inhibitors and Prostaglandin Analogues

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 31.3.1 Identify the characteristics of mucosal protectants and prostaglandin analogues used to treat gastrointestinal disorders.
- 31.3.2 Explain the indications, action, adverse reactions, and interactions of mucosal protectants and prostaglandin analogues used to treat gastrointestinal disorders.
- 31.3.3 Describe nursing implications of mucosal protectants and prostaglandin analogues used to treat gastrointestinal disorders.
- 31.3.4 Explain the client education related to mucosal protectants and prostaglandin analogues used to treat gastrointestinal disorders.

Mucosal Protectants

Pepsin is a gastric enzyme that breaks down and supports the digestion of proteins from foods. A low gastric pH of 1.5–2 activates pepsin. However, pepsin may cause erosive damage to the mucosal lining of the stomach. To mitigate the potential harm caused by pepsin, mucosal protectants are employed. These agents serve a dual purpose by reducing both gastric acid production and pepsin activity. Notably, when the gastric pH exceeds 5, mucosal protectants act as inhibitors of pepsin further safeguarding the delicate mucosal lining of the stomach.

Sucralfate

Sucralfate is classified as a mucosal protectant or coating agent. When ingested, it transforms into a viscous substance that adheres to ulcerated areas, creating a protective barrier on the mucosal lining of the stomach and duodenum. This protective paste-like barrier can adhere or stick to the ulcers for up to 6 hours, shielding them from the damaging effects of pepsin and hydrochloric acid. Sucralfate is especially effective with duodenal ulcers, ulcers due to aspirin use, and chemotherapy-induced mucositis. It may also be beneficial for stress ulcer prophylaxis.

Sucralfate is available in a tablet form or a liquid suspension. To maximize effectiveness, it should be taken 4 times a day, approximately 60 minutes before meals and at bedtime. When used alongside antacids in antiulcer therapy, it's advisable to administer antacids 30 minutes before or after sucralfate. Additionally, due to its adhesive properties, sucralfate should be taken at least 2 hours before or after medications such as quinolones, digoxin, phenytoin, and tetracycline to prevent any interference with their effectiveness.

Table 31.8 is a drug prototype table for sucralfate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Mucosal protectant, coating agent **Mechanism of Action** Locally reacts with hydrochloric acid and pepsin in the stomach to form an adherent protective paste-like substance capable of acting as an acid buffer	**Drug Dosage** 1 g orally 4 times daily for 4–8 weeks unless healing has been demonstrated by x-ray or endoscopic exam.
Indications Short-term treatment of active duodenal ulcers **Therapeutic Effects** Protects damaged gastric mucosa from further damage caused by pepsin and hydrochloric acid	**Drug Interactions** Cimetidine Digoxin Fluroquinolones Ketoconazole Phenytoin Quinidine Ranitidine Tetracycline Theophylline **Food Interactions** No significant interactions Sucralfate should be taken on an empty stomach
Adverse Effects Diarrhea Dry mouth Flatulence Nausea Pruritus Rash Dizziness Insomnia Headache Back pain Hyperglycemia	**Contraindications** Hypersensitivity Caution: Chronic kidney failure or dialysis secondary to risk of aluminum accumulation

TABLE 31.8 **Drug Prototype Table: Sucralfate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Prostaglandin Analogues

Prostaglandins are naturally occurring compounds present in the GI tract that protect the mucosal lining of the stomach and duodenum. They do this by inhibiting gastric acid and pepsin secretions.

Synthetic prostaglandin analogues, in a similar manner, act as mucosal protectants by decreasing acid secretions while increasing the secretion of bicarbonate and protective mucus. This combined action serves to fortify the defense mechanisms of the GI tract, preserving its delicate mucosal integrity.

Misoprostol

Misoprostol acts as an endogenous prostaglandin in the GI tract. As an antiulcer agent for the prevention of NSAID-induced ulcers, it inhibits basal and nocturnal gastric acid and pepsin secretions and also increases the secretion of bicarbonate and protective gastric mucous. Misoprostol also promotes vasodilation to maintain submucosal gastric blood flow. These actions prevent gastric ulcers.

Misoprostol is available in tablets that are administered with food 4 times a day alongside NSAID therapy. Misoprostol is readily available from the GI tract with an extensive first-pass metabolism, reaching peak levels in

60–90 minutes, with a brief half-life of 20–40 minutes.

Table 31.9 is a drug prototype table for misoprostol. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Prostaglandin analogue **Mechanism of Action** Acts as a synthetic prostaglandin E1 analogue with both antisecretory and mucosal protective properties in response to various gastric stimuli (meals, histamine, pentagastrin, and coffee)	**Drug Dosage** 200 mcg 4 times daily with food; if dose is not tolerated, a dose of 100 mcg can be used.
Indications Prevention of NSAID-induced gastric ulcers **Therapeutic Effects** Inhibits both basal and nocturnal gastric acid secretions	**Drug Interactions** Oxytocin **Food Interactions** No significant interaction
Adverse Effects Diarrhea/constipation Abdominal pain Dysmenorrhea/spotting Uterine contractions Postmenopausal bleeding Flatulence Headache	**Contraindications** Hypersensitivity to prostaglandins Pregnancy Caution: Cardiovascular disease People of childbearing age

TABLE 31.9 **Drug Prototype Table: Misoprostol** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects of mucosal protectants include hyperglycemia, dizziness, insomnia, and GI symptoms such as nausea, vomiting, diarrhea, and flatulence. Contraindications include hypersensitivity.

Typical adverse effects of prostaglandin analogues include headache, diarrhea or constipation, abdominal pain, flatulence, and gynecological symptoms such as **dysmenorrhea**, vaginal bleeding, uterine contractions, and postmenopausal bleeding. Contraindications include hypersensitivity to prostaglandins and pregnancy. Misoprostol may endanger pregnancy (may cause abortion) and cause harm to the fetus when administered to a pregnant client.

Nursing Implications

The nurse should do the following for clients who are taking mucosal protectants and prostaglandin analogues:

- Prior to administering, assess the client's medical history, current drug list, and allergies.
- Educate the client regarding short-term duration of use for these medications, typically 4–8 weeks.
- Inform clients of childbearing age about the potential risk to the fetus, which could result in a miscarriage.
- Provide the client with teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a mucosal protectant and prostaglandin analogue should:

- Adhere to the dosing regimen prescribed by the health care provider, typically short-term administration of 4–8 weeks.
- When using misoprostol, report symptoms of abnormal vaginal bleeding or uterine cramping to the health

care provider as these can represent serious adverse effects.

The client taking a mucosal protectant and prostaglandin analogue *should not:*

- Use prostaglandin analogues if pregnant due to the risk of fetal demise.

FDA BLACK BOX WARNING

Misoprostol

Misoprostol can cause spontaneous abortion, premature birth, or birth defects.

Chapter Summary

This chapter focused on various symptoms that may affect the gastrointestinal (GI) tract. The most common symptoms include heartburn, burning abdominal pain, and regurgitation, and they are often related to excess acidity in the GI tract. Other GI symptoms were discussed, such as bloating, a feeling of fullness, abdominal discomfort, belching, cough, nausea, and vomiting, which may occur simultaneously and may require a multifactorial approach to diagnosis and treatment. The chapter discussed different medications that may be prescribed for treatment and maintenance of these conditions. Nursing assessment and client education is imperative to the proper diagnosis and treatment of hyperacidic conditions.

Key Terms

agranulocytosis a life-threatening condition with severely low levels of neutrophils

alopecia loss of hair usually of the scalp in round patches, but may occur anywhere on the body where hair normally grows

antacids medications that neutralizes excess stomach acid

arthralgia a painful joint

dysmenorrhea painful menstrual periods and cramps

gastroesophageal reflux disease (GERD) a condition in which acidic gastric fluid flows backward into the esophagus, resulting in frequent dyspepsia/heartburn

gynecomastia an overdevelopment or enlargement of breast tissue in males

hydrochloric acid (HCl) a strong acid that is a component of gastric juices

hyperacidity a condition in which the level of gastric acid/hydrochloric acid is excessive, causing GI discomfort

neutropenia abnormally few neutrophils in the blood, leading to possible infection; an undesirable side effect of some cancer treatments

pepsin a digestive enzyme produced by cells in the stomach lining

peptic ulcer disease (PUD) open sores that develop on the inside lining of the stomach and the upper portion of the small intestine from excessive acid or corrosive chemicals/medications

prostaglandins a naturally occurring compound in the body that protects the stomach lining from acid

rebound hyperacidity the production of additional acid after the effects of an antacid wear off

tetany a condition in which the body experiences intermittent muscle spasms

transaminase an enzyme that helps with breakdown and metabolism of amino acids

Zollinger-Ellison syndrome a rare medical condition characterized by excessive production of stomach acid

Review Questions

1. A client in the clinic is prescribed aluminum hydroxide by the provider. The nurse should include which of the following in the client's education?
   a. Take the medication 2 hours before or after other medications.
   b. This medication will put you at risk for respiratory infections like pneumonia.
   c. Stop taking this medication if constipation develops.
   d. You will need lab work to check your blood level of magnesium.

2. The nurse is administering IV cimetidine to a client admitted to the ICU with a GI bleed. Which of the following adverse effects is the client at increased risk for when receiving cimetidine parenterally?
   a. Gynecomastia
   b. Confusion
   c. Agranulocytosis
   d. Hypotension

3. The nurse is educating a client on a new prescription of omeprazole. What does the nurse include in teaching?
   a. The medication is best administered at bedtime.
   b. The medication decreases the production of gastric acids and pepsin.
   c. The medication is best taken 2 hours after a meal.
   d. The medication may cause hyperkalemia.

4. The nurse is educating the client on their newly prescribed medication misoprostol. Which of the following

statements by the client indicates a priority need for additional follow-up?

a. "I recently stopped taking my birth-control pills."
b. "I am taking a prescription-strength NSAID 3 times a day for my knee pain."
c. "I am worried taking this will cause gas and diarrhea."
d. "I need to remember to take this medication with food."

5. A client being treated for GERD arrives at the clinic with complaints of constipation and flatulence. Which of the following medications is likely causing these symptoms?

a. Magnesium hydroxide
b. Calcium carbonate
c. Simethicone
d. Docusate sodium

6. The nurse is discharging a client with instructions from the provider to take calcium carbonate to treat their indigestion. Which of the following statements by the client indicates the need for additional instruction?

a. "I shouldn't take this when I take my other medications."
b. "I should take this only when I have symptoms."
c. "I need to take this after meals and at bedtime."
d. "I need to take this every day for it to work."

7. The nurse is preparing to administer a dose of lansoprazole to a client with an ulcer. Which of the following statements by the client indicates the client needs additional instruction on this medication?

a. "I know my pain will improve right after taking this."
b. "I need to take this every day before a meal."
c. "I understand it can take about 6 months to experience the full benefit of this medication."
d. "I hate the thought of having to take this for the rest of my life."

8. The nurse is providing discharge instructions to a client with a gastric ulcer who is taking sucralfate. What information regarding administration is important to stress to the client?

a. Take this medication 4 times a day; do not miss a dose.
b. Limit dietary fiber and fluids.
c. Take with an antacid as needed.
d. It is safe to take before dialysis.

9. The nurse is reviewing lab values for a client who has been taking over-the-counter antacid medications. Which of the following findings could be attributed to antacid use?

a. Hypocalcemia
b. Hyperphosphatemia
c. Hyponatremia
d. Hypermagnesemia

10. The nurse is educating a client who is taking pantoprazole. What information should be included in the education?

a. Stop taking this medication if you have a headache.
b. You will need this medication for the rest of your life.
c. Swallow the medication whole, do not chew.
d. Plan to take this medication only with meals.

CHAPTER 32
Weight Management Drugs

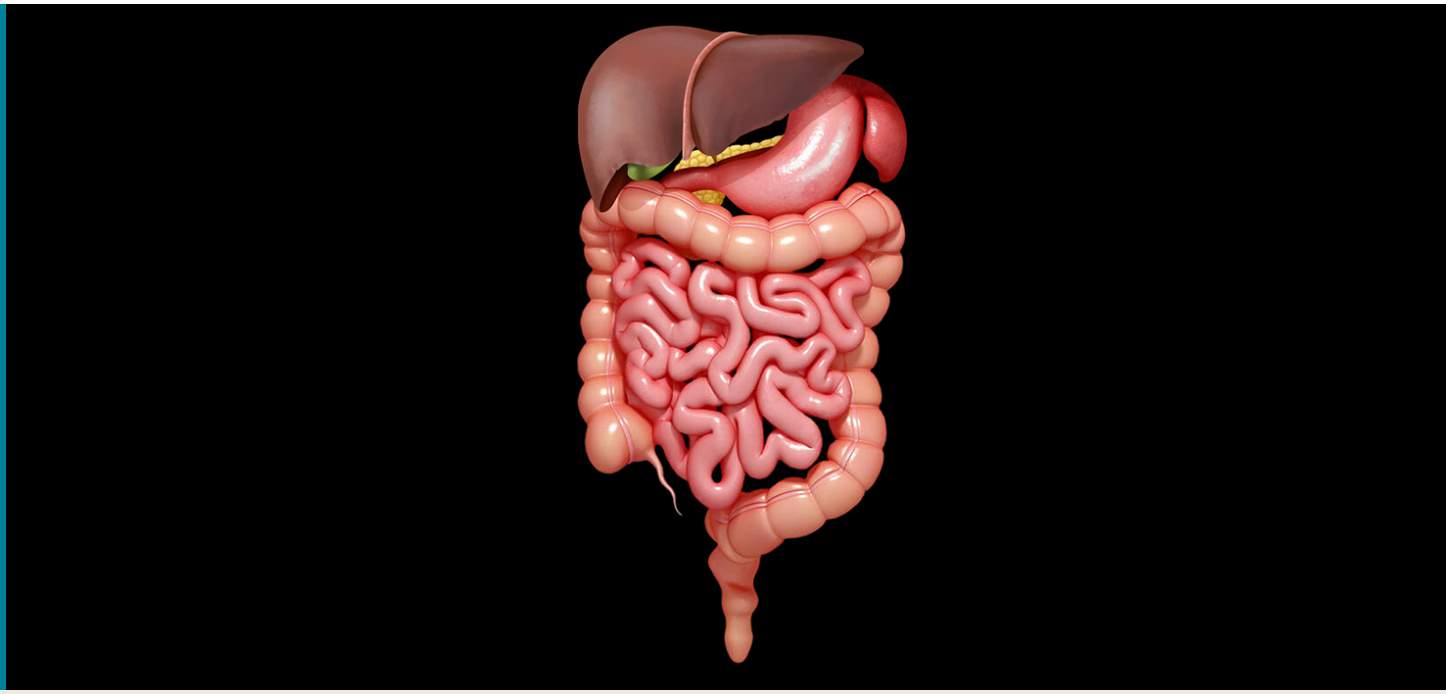


FIGURE 32.1 The digestive system breaks down food into nutrients that can be absorbed into the bloodstream to give the body energy and the ability to grow and repair itself. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION In the United States, almost 75% of adults age 20 or older are classified as having overweight or obesity based on their body mass index (BMI). Almost 20% of children ages 2–19 live with obesity (National Heart, Lung, and Blood Institute, 2022). According to the World Health Organization, over the past 50 years the global incidence of obesity has tripled (Yadav & Jawahar, 2023). The body of evidence notes that disparities exist by race and ethnicity, age, educational level, and environmental factors. Maintaining a healthy weight can reduce many health risks, especially those associated with obesity such as diabetes, hypertension, and cardiovascular disease. Overweight and obesity may lead to various serious health issues for people of all ages. An alarming consequence is the monetary impact affecting people with overweight and obesity. According to the Centers for Disease Control and Prevention (CDC, 2022b), obesity-related medical costs in the United Sates were an estimated $173 billion annually (about $530 per person in the United States). The ramifications also include a loss of productivity due to absenteeism. The CDC estimates that the national loss of productivity costs between $3.4 and $6.4 billion annually (about $20 per person in the United States).

The detrimental consequences of overweight and obesity on the health and wellness of people, compounded with financial burdens, lead to a critical need for weight management. Proper weight management starts with understanding the pathophysiology of overweight and obese conditions and the comorbidities. This understanding must also consider genetic and lifestyle factors to promote optimal weight management. Pharmaceutical agents to promote weight loss and bariatric procedures may be initiated when lifestyle and behavioral modifications are ineffective at maintaining a healthy weight. All of these aspects will be discussed in this chapter.

32.1 Introduction to Weight Management

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 32.1.1 Describe the pathophysiology of overweight and obesity.
- 32.1.2 Identify clinical manifestations related to obesity.
- 32.1.3 Identify the etiology and diagnostic studies related to obesity.
- 32.1.4 Describe nonpharmacologic measures to reduce weight.

Overweight and **obesity** are terms that can be used to describe the increase in the size and number of fat (**adipose**) cells in the body. There are two ways that adipose tissue increases in the body. **Hyperplasia** of adipose tissue is an increase in the number of fat cells in the body. **Hypertrophy** is an increase in the size of fat cells. Both genetics and lifestyle, mainly a diet high in fat, affect hyperplasia and hypertrophy of adipose tissue. There is a strong correlation between genetics and adipose tissue growth. Adipose tissue begins to develop in a fetus by the second trimester. Despite a genetic predisposition, lifestyle behaviors can impact developing overweight or obesity.

Simply stated, excess weight gain that can lead to overweight or obesity can be caused by ingesting more calories than the body needs to function. The American Heart Association (2020) notes that a healthy diet that includes fruits, vegetables, whole grains, low-fat dairy products, and lean proteins low in saturated fats reduces the risk of cardiometabolic diseases in the United States. However, there are many reasons why people ingest more calories than what is needed by the body. One major factor is the increased availability and consumption of highly processed convenience foods. These foods are often high in sugar and fat. Unfortunately, high-calorie, high-sugar, high-fat, processed foods are often less costly than healthier foods. People struggling with finances or living in a **food desert** (an area where people have extremely limited access to healthy, affordable food) often buy low-cost, high-sugar, high-sodium, and high-fat foods that are cheaper than healthy food choices.

Obesity is recognized as a complex medical condition. In addition to diet, there are other factors that can increase the likelihood of a person developing obesity, including genetics, lack of sleep, decreased or restricted physical activity, certain medications, and stress. Obesity raises an individual's risk for developing heart disease, hypertension, diabetes, and cancer (National Heart, Lung, and Blood Institute, 2022).

Weight Stigma

Society typically values a person who is "thin and fit," despite the fact that almost 75% of Americans live with overweight or obesity. Obesity stigma is characterized by prejudice, stereotyping, and discriminating bias and actions toward people with obesity, often fueled by inaccurate ideas about the causes of obesity (Westbury et al., 2013). **Weight stigma** often stereotypes people with overweight or obesity negatively as lacking self-discipline, being lazy or sloppy, and lacking intelligence. These stereotypes may result in discrimination in relationships, social acceptance, employment, and recognition. Weight discrimination often leads to adverse health consequences such as binge eating, psychological and physiological stress, weight gain, and avoidance of participating in healthy behaviors and provider follow-up (Lee et al., 2021). Weight stigma may be internalized by the person with overweight or obesity. Unfortunately, clients may encounter weight stigma as a bias among health care professionals (American College of Obstetricians and Gynecologists, 2019). However, individuals may have their own phrasing and preferences for how they discuss their body size, health, and weight, and nurses should consider those preferences as well.

Overweight and obesity are medical conditions. As with all medical conditions, health care professionals should approach these conditions with a focus on a client-centered treatment plan. Physicians, nurses, physical therapists, nutritionists, and fitness professionals are a few of the types of health care professionals who have contributed to weight bias, stigma, and discrimination by labeling people with overweight and obesity as "noncompliant," furthering the weight stigma (World Obesity Federation, n.d.). How health care professionals engage in conversations and use terminology with clients is vital to avoid further bias and weight stigma. Using person-first terms such as "person with obesity" instead of "obese person" is recommended for health care professionals. The first term identifies the client as having a condition rather than defining the person as obese. The terms "morbidly obese," "fat," and "obese" have been found to be the most stigmatizing, whereas "weight problem," "unhealthy weight," and "high BMI" have been found to be the most motivating and least offensive language options for discussing weight with clients (American College of Obstetricians and Gynecologists, 2019).

In addition to being thoughtful in their verbal communications, health care professionals can decrease weight stigma by implementing individualized client-centered weight counseling, encouraging healthy lifestyle behaviors, displaying empathy, and being supportive. Above all, health care professionals should treat overweight and obesity as a medical condition requiring an interprofessional, individualized treatment plan. Nonpharmacological modalities such as meal planning and increased physical activity are encouraged before moving on to weight-loss drugs and bariatric procedures or surgeries. Health care professionals should focus on the consequences, complications, and comorbidities of overweight and obesity, while being certain that they are not simply promoting a "thin body ideal." For example, health care professionals should not assume that a person with overweight or obesity is unable or unwilling to participate in certain activities, such as physically challenging events. And healthcare professionals should never assume or imply that people with overweight or obesity should be unhappy in their bodies.

Overweight Versus Obesity

Overweight and obesity both are defined as abnormal or excessive fat accumulation that may impair health. However, overweight and obesity are not the same thing.

Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. For adults, the World Health Organization (WHO) defines overweight as a BMI greater than or equal to 25 and obesity as a BMI greater than or equal to 30 (WHO, 2021). Being overweight may change the way the body functions and may lead to adverse health effects. If the body is overweight for a prolonged period, it progressively may lead to obesity (Mayo Clinic, 2023c).

Body fat alone is not a disease. In fact, the human body requires fat for energy and to function. Body fat insulates and protects vital organs. The body cannot produce fat on its own. It is essential for humans to ingest cholesterol, triglycerides, and essential fatty acids (EFAs) for basic metabolic and immune functions and to supply the body with the fat-soluble vitamins A, D, E, and K (MedlinePlus, 2023). Despite the importance of fats in the human body, regulation is key to avoiding developing overweight or obesity.

Body Mass Index

The BMI is calculated for adults by first determining a person's height and weight. The weight in pounds is divided by the height in inches and then multiplied by a conversion factor of 703 to obtain the BMI. To determine the BMI using the metric system, divide the weight in kilograms by the height in square meters and then multiply the result by 10,000. Although the BMI is calculated in the same way for children and teens, clinicians interpret the findings for them differently. For children and adolescents, refer to the CDC Growth Charts (https://openstax.org/r/growthcharts).

BMI for adults 20 years and older (see Figure 32.2):

- Healthy weight: 18.5–24.9 kg/m^2
- Overweight: 25.0–29.9 kg/m^2
- Obese: 30.0 kg/m^2 and greater

These parameters may not apply to athletes, body builders, or people who exercise a lot because a BMI may be higher in athletes due to their increased muscle mass. Also, BMI measurements are based on anthropometric measurements of White people. Body fat distribution differs by race and ethnicity, such as among Hispanic, Black, East Asian, and South Asian populations (Nair, 2021). The BMI interpretations should be adjusted based on ethnicities (Harvard T. H. Chan School of Public Health, n.d.). Furthermore, the American Medical Association indicates that BMI should not be used as a sole determinant of health and risk. Rather, it should be used in conjunction with measurements of body adiposity index, relative fat mass, waist circumference, and visceral fat, as well as considerations of body composition, genetic factors, metabolic factors, and other measures (American Medical Association, 2023).

The significance of an increased BMI should be determined by a health care professional and discussed with clients on an individual basis. When obesity is determined to be detrimental to health, it is further classified as:

- Class I obesity: 30–34 kg/m^2
- Class II obesity: 35–39 kg/m^2
- Class III obesity: 40+ kg/m^2

Treatment for obesity is often determined by the class of obesity the client fits into, as determined by a health care professional. Class III obesity is most often linked to serious health conditions.

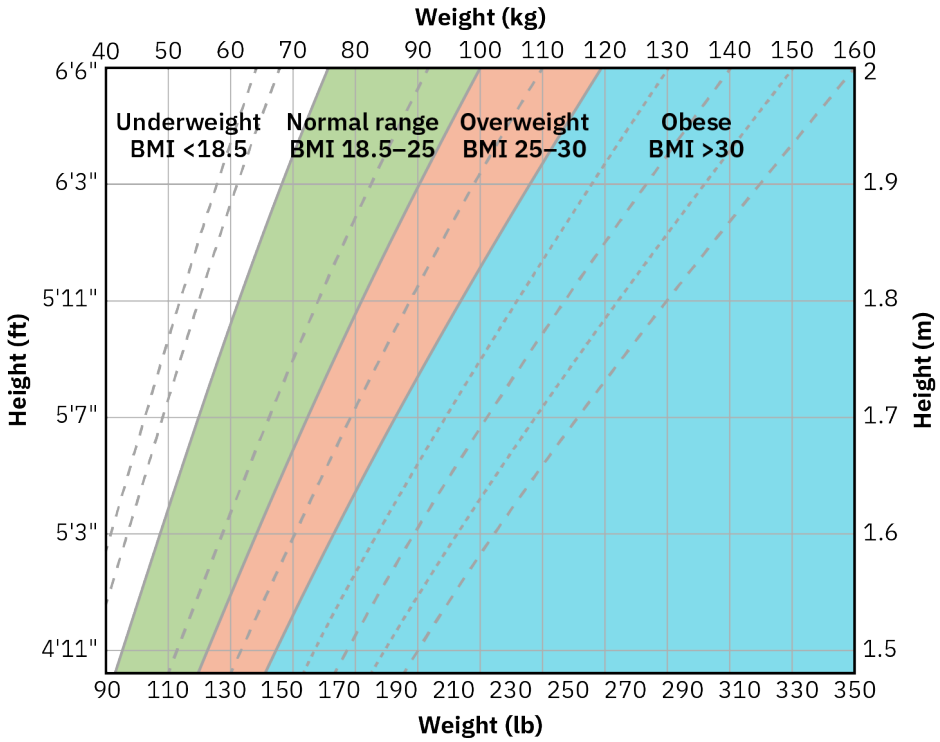


FIGURE 32.2 This chart is a simple way to calculate BMI for adults based on height and weight in kilograms. BMI should be used as one evaluation in conjunction with other measures of health. (credit: modification of work from *Psychology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Factors Associated with Obesity

Obesity at a minimum alters the body's metabolism. Metabolism is the body's process of converting calories into energy for optimal functioning. When the body takes in too many calories, it stores the excess as adipose tissue. Excess adipose tissue secretes hormones that start an inflammatory process in the body that may lead to chronic inflammation and **insulin resistance**. With insulin resistance, the body does not respond to insulin to properly regulate blood glucose levels. This affects the body's ability to use glucose for energy in the muscles and other body organs, and glucose builds up in the bloodstream (hyperglycemia). The pancreas then does what it is supposed to do and produces more insulin to combat hyperglycemia. Over time, this circle leads to type 2 diabetes mellitus. Obesity raises the incidence of developing type 2 diabetes 7–12 times that of a person of a healthy weight (Cleveland Clinic, 2022).

Hormonal weight gain due to aging is another concern, especially for postmenopausal clients. According to Mayo Clinic (2023d), hormonal changes due to menopause may cause up to 1.5 pounds of weight increase, particularly in the abdominal area. However, an active lifestyle and healthy eating patterns can minimize postmenopausal weight gain.

In addition to hyperglycemia from chronic inflammatory processes and insulin resistance, serum lipids (cholesterol and triglycerides) may increase, leading to hyperlipidemia. The combination of hyperglycemia and hyperlipidemia leads to hypertension (high blood pressure). These risk factors are often grouped together in a condition called **metabolic syndrome**, which is a collection of risk factors, including overweight and obesity, that drastically increases the chance of a person developing hypertension, diabetes, heart disease, and stroke. In addition to steering the body to metabolic syndrome, increased BMI coupled with hyperglycemia, hyperlipidemia, hypertension, and/or chronic inflammation increases the risk of atherosclerosis, cardiovascular disease, and coronary artery disease. As metabolic syndrome may be prevented with client education on nutrition and meal planning, it is recommended that providers consider referring clients to a registered dietician for individual meal planning education.

The excess circulating serum lipids and glucose eventually make their way to the liver, kidneys, and gallbladder. The liver and kidneys are responsible for filtering the blood. Excessive lipids in the liver may lead to **steatosis** and nonalcoholic fatty liver disease (NAFLD). Long-term storage of excess lipids in the liver can increase chronic inflammation in the liver, triggering hepatitis and eventually possible cirrhosis. Prolonged hyperglycemia and hypertension are taxing on the kidneys and eventually affect the functioning of the renal tissue, leading to possible chronic kidney disease. High cholesterol can also accumulate in the gallbladder, leading to **cholelithiasis**, which further impairs metabolism.

In addition to the metabolic issues that can lead to serious chronic diseases, overweight and obesity have detrimental direct effects on the body due to the excess adipose tissue. The strain primarily affects the musculoskeletal and respiratory systems. The excess weight on the musculoskeletal system impairs the body's ability to support itself. It also impairs mobility. The added weight on the soft tissues, bones, joints, tendons, and ligaments causes stiffness and pain. This may lead to injuries and diseases such as low back pain, osteoarthritis, and gout, further impeding mobility.

Excess body fat also puts additional strain on the respiratory system, contributing to **obesity hypoventilation syndrome**, **sleep apnea**, and asthma. Obesity hypoventilation syndrome (OHS) is a respiratory condition that is a direct outcome of obesity, especially Class III obesity. "OHS is defined by the combination of obesity (body mass index [BMI] ≥30 kg/m^2), SDB [sleep-disordered breathing], and awake daytime hypercapnia (awake resting $PaCO_2$ [the partial pressure of carbon dioxide] ≥45 mm Hg at sea level), after excluding other causes for hypoventilation" (Mokhlesi et al., 2019).

Physiological Factors

Physiological factors are related to the chemical and physical processes that occur within the body. Various physiological factors affect weight management including basal metabolic rate (BMR), circadian rhythm and sleep cycles, hormones, thermogenesis, physical fitness and strength, digestive health and gut flora, prenatal and postnatal factors, and physiological response to stress. The foundational physiological factor in weight management is the BMR, which is the amount of energy required to sustain the essential body functions of life. The physiology of the BMR is influenced by several factors including sex, muscle mass, body size, amount of sleep, and genetics. Males have a greater BMR than females, which accounts for the muscle mass and fat distribution differences. Muscles burn about 4 calories more per hour than adipose tissue. Although males have a greater muscle mass than females, it is important for females to maintain a proper proportion of lean muscle mass to maintain a higher BMR.

An adequate amount of sleep is fundamental for maintaining physical, psychological, and emotional health. For optimal health, 7–9 hours of sleep per night is recommended. Sleep is essential to proper weight management. Poor sleep is associated with glucose intolerance and insulin resistance. Additionally, sleep deprivation affects metabolic rates, hormones that regulate metabolism, and even eating habits (Papatriantafyllou et al., 2022). The effects of sleep on worsening obesity have been studied quite a bit in children. Results demonstrate that just 1 hour less sleep per night from normal sleep patterns can lead to an increase in obesity in children and teens (Yadav & Jawahar, 2023).

It is important to pay attention to an individual's internal clock (**circadian rhythm**) in respect to sleep as well. Hormonal regulation affecting eating and sleeping is controlled by a person's physiological circadian rhythm. Not paying attention to the urge to sleep based on the physiological internal clock can alter weight management. Incidentally, eating too late at night can not only alter the circadian rhythm but also interfere with sleep (Reynolds, 2022).

Several hormones play a role in weight management, influencing appetite and the ability to utilize adipose tissue as an energy source. **Insulin**, an anabolic hormone, regulates glucagon and fat for energy. **Ghrelin** is a hormone that controls hunger and satiety. **Leptin** is another hormone that is primarily involved in satiety. According to the Cleveland Clinic (2023a), research demonstrates that some people may have **leptin resistance**, which may lead to weight gain by inhibiting satiety, increasing hunger, and decreasing metabolism. **Glucagon** is a hormone that stimulates hepatic glucose production (gluconeogenesis). Weight gain is promoted when insulin and ghrelin are chronically elevated and leptin and glucagon are chronically low. Many factors affect this cycle, including sleep deprivation.

Thermogenesis is an integral process of the body's metabolic functions. It is the production of heat in the human

body, specifically in brown adipose tissue and skeletal muscle. Thermogenesis burns calories to produce heat/energy, creating a negative energy balance that leads to weight loss. It is sometimes referred to as "fat burning" due to the burning of specifically adipose tissue. There are three primary types of thermogenesis: nonexercise-activity thermogenesis (NEAT), exercise-associated thermogenesis (EAT), and diet-induced thermogenesis (DIT). NEAT occurs under normal natural physical activity and burns calories associated with activities of daily living. EAT refers to calories that are burned with purposeful exercise. DIT is the production of heat (calorie burning) that occurs after eating. Intentionally increasing thermogenesis is a nonpharmacological method of weight management (discussed later in the chapter).

Genetic Factors

In terms of factors affecting obesity, heredity and genetic factors have been considered part of a multifactorial cause. Genome studies demonstrate genetic biological reinforcement and the role of the brain in weight management (Loos & Yeo, 2021). Genes affect the amount of fat stored in an individual's body and fat distribution. Several genes play a role in the pathogenesis of overweight and obesity. The most significant is the fat mass and obesity-associated (FTO) gene. Genetic variation in the first segment of the FTO gene is largely related to adiposity. This may lead to long-term overweight and obesity consequences as an adult (Huang et al., 2023). Genetics may also play a role in digestion and metabolism; however, genetics are not the sole cause of obesity.

Ethnicity has also been correlated with excess weight. Non-Hispanic Black adults (49.9%) had the highest age-adjusted prevalence of obesity, followed by Hispanic adults (45.6%), non-Hispanic White adults (41.4%), and non-Hispanic Asian adults (16.1%) (CDC, 2022c). There is some evidence that the differences may be linked to racial genetics that affect body composition and fat distribution.

Environmental Factors

In most discussions about the genetic influences of obesity, the role of family environment is also stressed as a major factor of obesity. Family environment may lead to sedentary and poor lifestyle behaviors. There may also be socioeconomic factors related to the family environment. In the United States over the last few decades, there has been an increased incidence of choosing ultra-processed and fast food for meals. This is coupled with a decrease in physical activity, especially in children. Food deserts are also a concern with weight management. Healthy food accessibility is a major environmental factor, especially in lower-income and minority neighborhoods, which have approximately 30% fewer supermarkets (Yadav & Jawahar, 2023).

The family environment also greatly influences lifestyle behaviors such as physical activity, eating behaviors, sleep patterns, and reactions to stress. All of these can affect weight management. Physical spaces such as where one lives, works, and socializes have a large familial influence and can affect weight management. Gurka et al. (2018) found that the prevalence of obesity fluctuates across the United States based on geographic areas. The highest levels of obesity, diabetes, and metabolic syndrome in the United States are in the Midwest and Southern regions.

Psychological Factors

According to the National Council on Aging (Vafiadis, 2021), research demonstrates that there are barriers to treatments based on the complex interrelatedness between obesity and mental health. Most discussions on obesity focus on the physical consequences such as cardiovascular challenges, type 2 diabetes, and musculoskeletal conditions. Rarely are the emotional and mental health impacts related to obesity considered in treatment plans (Vafiadis, 2021). There are significant psychological burdens associated with obesity and its comorbidities. People with obesity often exhibit more self-esteem issues, body-image dissatisfaction, anxiety, depression, low quality of life, and discrimination (Vafiadis, 2021).

Due to the large body mass from obesity and the detrimental effects of comorbidities, people with obesity often are unable to participate in activities they enjoy, such as spending time with family and friends, traveling, attending social events, or participating in hobbies. Social isolation may lead to loneliness, difficulty coping, and depression. Furthering the potential for depression is society's negative attitude toward overweight and obesity. People with obesity often experience **weight bias**, being stereotyped as lacking self-discipline or being lazy. Weight bias may also be present among health care providers (American College of Obstetricians and Gynecologists, 2019). These critical biases may lead to discrimination. Discriminatory behaviors and weight bias may exacerbate depressive symptoms.

There is a reciprocal relationship between obesity and mental health concerns. Although overweight and obesity

may trigger consequences on mental and emotional health, various mental and emotional conditions may, in turn, lead to behaviors causing weight gain. Chronic stress, anxiety, depression, and bipolar disorder may cause a person to use food for comfort or decrease their interest in participating in physical activities. Self-medication with food is common in clients with depressed mood, sleep disturbances, and anxiety due to **serotonin deficiency** (Vafiadis, 2021). Serotonin is a vital neurotransmitter for optimal functioning of body processes, enhancing learning, memory, and happiness. Serotonin also regulates sleep, mood, digestion, satiety, bone health, wound healing, and sexual desires. When there is an imbalance of serotonin, physical and psychological symptoms such as depression, mania, and anxiety may occur (Cleveland Clinic, 2023b). The complex interrelationship between obesity and mental health requires further exploration of the connections and weight-management strategies.

Nonpharmacologic Weight Management

Obesity is an epidemic worldwide caused by biological, genetic, social, environmental, and behavioral factors. There is no single treatment or easy solution to reducing overweight and obesity; it is a multifaceted dilemma requiring comprehensive multidimensional approaches that are individualized to the client. Weight reduction focuses on meal planning and increasing physical activity to reduce weight, thus preventing or reducing obesity complication. Nonpharmacological weight-loss strategies, such as behavioral lifestyle interventions of eating less and moving more, should be initiated before drugs and/or procedures. Collaborative short-term weight-management and behavioral goals should be developed with an experienced health care professional in weight management. Client education and support are vital to weight-loss and management success.

A healthy meal plan should be balanced with moderate lean proteins and complex carbohydrates and should be low in fat and sugar. Foods with a **glycemic index (GI)** of less than 55 are recommended to promote stable blood glucose levels that aid in weight management. Foods in this category include most fruits and vegetables, beans, minimally processed grains, pasta, low-fat dairy foods, and nuts (Harvard Health, 2023).

Lean-protein foods such as fish and poultry increase the basal metabolic rate while balancing the release of insulin and serum glucose levels. This results in glucagon mobilizing adipose tissue and promoting more weight loss. A consistent eating schedule also enhances constant blood glucose levels. Controlling blood glucose levels enhances the body's ability to burn stored body fat while controlling hunger.

Eating many raw fresh fruits and vegetables is recommended to increase dietary fiber and promote clean eating. **Clean eating** refers to eating foods that are in their natural state and unprocessed because these are **nutrient-dense foods** and free of synthetic chemicals, preservatives, and additives such as sugar and salt (Dutter, 2019). These additives are detrimental to health and often promote weight gain. Choosing foods that the client likes will encourage adherence. Individual considerations must be taken into account to provide optimal nutrition, promote weight loss, and ensure success. Eating fewer calories and increasing physical activity coupled with behavior modification is the only way to lose weight. However, clients must be educated on eating the right foods in a collaborative weight-management plan determined with a health care professional.

The **Mediterranean diet**, which is high in fish (especially those species high in omega-3 fatty acids), fresh fruits and vegetables, whole grains, nuts, and olive oil, has been shown to reduce the risk of cardiovascular disease and metabolic syndrome while promoting weight loss. Extra virgin olive oil is the main source of dietary fat in a Mediterranean diet.

Some foods that help boost metabolism and quickly burn body fat are classified as **thermogenic foods**. Proteins are considered a thermogenic food because the digestion process takes the longest and burns more calories. High-protein foods incorporated into a daily meal plan help with weight loss by burning more calories. Plant-based proteins such as lentils, chickpeas, black beans, hemp seeds, nuts, quinoa, tofu, and peanut butter help to increase metabolism. Lean animal proteins such as poultry (white meat), fish (salmon, tuna, mackerel, herring, and sardines), pork tenderloin, lean beef cuts, and eggs curb hunger while promoting thermogenesis. Caffeine and green tea are excellent additives in a meal plan for thermogenesis. Other foods to enhance thermogenesis are coconut oil, ginger, and capsaicin/red pepper. High-fiber foods also help increase thermogenesis.

Supplements such as garcinia cambogia, yohimbine, and bitter orange may also promote thermogenesis (National Institutes of Health, 2022). Other supplements that help with weight loss and management include:

- *Chromium picolinate:* Stabilizes metabolism of carbohydrates (reduces sugar cravings)

- *Essential fatty acids (EFAs):* Provide cellular nutritional support and appetite control
- *Amino acids:* Decrease cravings and promote weight loss
- *Kelp:* Balances minerals and aids in weight loss
- *Spirulina:* Protein source, stabilizes blood glucose
- *Multivitamins:* Provide nutritional support
- *Herbs:* See Section 32.4 for more on herbal supplements

In addition to a healthy meal plan, increasing physical activity promotes weight loss. Adding an exercise program should be done in consultation with the client's health care provider and an exercise professional. Limiting sedentary activities is key to enhancing weight loss. If a reduction in caloric intake and increasing physical activity is ineffective after 12 months, drugs such as anorexiants, lipase inhibitors, and herbal supplements may be used to aid in weight loss.

CLINICAL TIP

Talk to Your Client

When discussing goals with a client who needs to lose weight, it is important to talk about all aspects of the client's life that affect weight management. Sustainable weight loss requires a comprehensive approach with a foundation on eating balanced, heart-healthy foods and getting consistent physical activity, along with adequate sleep and stress reduction.

TRENDING TODAY

Clinical Trials on Overweight and Obesity

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) has conducted clinical trials to prevent, detect, and treat overweight and obesity that lead to multiple system diseases. On its Health Information page, Clinical Trials for Overweight & Obesity (https://openstax.org/r/growthcharts), the NIDDK outlines how clinical trials may optimize weight management and overall health. Clinical trials are essential to help understand the best evidence-based strategies to prevent and minimize overweight and obesity.

SPECIAL CONSIDERATIONS

Weight-Loss Medications and Supplements

Individual factors such as age, sex, and ethnicity must be considered with the use of all weight-loss medications and supplements. Older clients may not be able to absorb and excrete drugs, leading to ineffective or toxic doses. Safety concerns for various racial/ethnic groups include differences in absorption, metabolism, distribution, and excretion due to genetic components and possible cytochrome P-450 (CYP) deficiencies. Additionally, nurses must assess the client's ability to understand and comprehend medication instructions and education.

(Source: National Institutes of Health, 2022)

32.2 Anorexiants

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 32.2.1 Identify the characteristics of anorexiant drugs used for weight management.
- 32.2.2 Explain the indications, actions, adverse reactions, and interactions of anorexiant drugs used for weight management.
- 32.2.3 Describe nursing implications of anorexiant drugs used for weight management.
- 32.2.4 Explain the client education related to anorexiant drugs used for weight management.

Anorexiants are drugs used to promote weight loss through appetite suppressant and stimulation effects by

increasing norepinephrine availability to neural receptors. Although these drugs have gone through the standard U.S. Food and Drug Administration (FDA) approval process, many have been removed from the market due to the critical and fatal effects of body stimulation.

Phentermine Hydrochloride

Phentermine hydrochloride is a sympathetic amine that stimulates the central nervous system to increase norepinephrine (NE) availability. When NE is attached to brain receptors, it suppresses the appetite and increases metabolism. Along with following a healthy diet, phentermine hydrochloride is used adjunctly as an oral tablet or capsule to promote weight loss. It is recommended for short-term therapy (8–12 weeks) as a daily dose or three times a day before meals.

Phentermine hydrochloride is a Schedule IV controlled substance because there may be a potential for problematic use; it should not be used for clients with a history of substance misuse or substance use disorder.

Phentermine and Topiramate ER

The drugs phentermine (an anorexiant and stimulant) and extended-release topiramate (an anticonvulsant and gamma-aminobutyric acid [GABA]) are combined in a capsule for weight management. It is utilized in addition to daily caloric restriction and increased physical activity in clients with an initial BMI of 30 kg/m^2 or greater *and* at least one other comorbidity of hypertension, type 2 diabetes mellitus, and/or dyslipidemia.

Clients are initially started on a low dose of the drugs for 14 days; the dose is then increased yet still taken once per day for 12 more weeks. Weight is assessed after 12 weeks of the increased dosage. If weight loss has not exceeded 3% of the baseline weight, the dose is either discontinued or increased again, with an increased dosing for another 14 days and increased again for 14 weeks. Baseline weight at that point is reassessed, looking for a 5% or more weight loss over baseline. Daily doses are not increased in clients with renal and/or hepatic insufficiency.

Phentermine and topiramate ER is also a Schedule IV controlled substance.

Phendimetrazine

Phendimetrazine is an appetite suppressant used short-term to promote weight loss in conjunction with a low-calorie diet and exercise in clients who did not lose weight with diet and exercise alone. The drug is available in immediate-release (IR) tablets, extended-release (ER) capsules, and sustained-release (SR) capsules. It is important to swallow the extended-release capsule whole. Clients should not crush, break, or chew it.

Dosage varies for each client. Clients should be educated to follow the prescribed dosage and instructions. Dosing is determined by the provider based on both the client's individual needs and the dosage form (Mayo Clinic, 2023a).

Nurses should advise clients that if they miss a dose, they should take it as soon as possible; however, if it is close to the time for the next dose, they should skip the dose. Clients should not take double doses. This medication is a stimulant and should never be increased without the provider's advice.

Benzphetamine

The drug benzphetamine is another CNS stimulant used as an anorexiant for weight loss in clients with obesity. Benzphetamine is an indirect sympathomimetic amine that acts like amphetamine, yet with fewer side effects. Its effectiveness as an appetite suppressant is thought to be due to the stimulating effects on the hypothalamus that release catecholamines. It is a Schedule III controlled substance for its potential for misuse and should not be used in clients with addictive behaviors.

Table 32.1 lists common anorexiants and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Phentermine (Adipex-P, Lomaira)	15–37.5 mg orally every morning. *Lomaira only:* 8 mg 3 times daily. Administer 30 minutes before meals or 1–2 hours after meals.
Phentermine and topiramate ER (Qsymia)	Initial dose: 37.5 mg/23 mg orally for 14 days, then increase to 7.5 mg/46 mg daily. Weight is assessed after 12 weeks for dosage adjustment based on weight loss.
Phendimetrazine	*150 mg ER or SR capsule:* Orally once daily 30–60 minutes before morning meal. *35 mg IR tablet:* Orally 2–3 times daily 60 minutes before meals; maximum dose: 70 mg/day.
Benzphetamine	25–50 mg orally 1–3 times daily; best in 1 single mid-day dose; do not administer within 6 hours before bedtime to avoid insomnia.

TABLE 32.1 **Drug Emphasis Table: Anorexiants** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

All four drugs discussed in this section should not be administered within 14 days of taking a monoamine oxidase inhibitor (MAOI), such as phenelzine, selegiline, isocarboxazid, or tranylcypromine. Using these medicines together may cause serious unwanted effects (Mayo Clinic, 2023b).

Use of phentermine hydrochloride is contraindicated in clients with hypersensitivity to sympathetic amines. The drug is a CNS stimulant, so it is often contraindicated in clients with hyperthyroid conditions, glaucoma, agitation, severe renal impairment, and/or cardiovascular disease such as coronary artery disease, stroke, arrhythmias, congestive heart failure, and uncontrolled hypertension (DailyMed, *Adipex-P*, 2020). Phentermine hydrochloride is used cautiously in clients with seizures, hypertension, diabetes mellitus, and renal impairment. Caution also should be exercised in clients with a history of substance use disorder because there is a risk of misuse with Schedule III and Schedule IV drugs.

Adverse effects of phentermine are related to the stimulant effects of the drug and include palpitations, tachycardia, arrythmias, precordial pain, nervousness, restlessness, dizziness, insomnia, anxiety, agitation, and tremors. Other adverse effects include hyper- or hypotension, syncope, pulmonary hypertension, fatigue, malaise, confusion, incoordination, headache, change in libido, gynecomastia, and hair loss. Severe hematological adverse effects are bone marrow suppression, agranulocytosis, and leukopenia. It is important to instruct clients not to take the drug late in the evening because it may cause insomnia.

Along with MAOIs, phentermine is contraindicated with tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), and antihypertensive drugs.

Life-threatening adverse drug reactions (ADRs) for phentermine and topiramate include hepatotoxicity and skin conditions such as Stevens–Johnson syndrome, erythema multiforme, and toxic epidermal necrolysis. Life-threatening seizures may occur following abrupt discontinuation of the drug. Clients should be monitored closely for changes in behavior, such as the development of or worsening depression and/or suicidal ideation.

Phentermine and topiramate ER combination is contraindicated in clients with hypersensitivity to either drug, sympathomimetics, or stimulants. It is also contraindicated in clients with glaucoma, hyperthyroidism, severe renal impairment, severe hepatic impairment, pregnancy, lactation, or history of suicidal ideation. Cautious use is recommended in clients with diabetes mellitus because there is a risk of hypoglycemia with weight loss. Clients with diabetes should be encouraged to speak to their provider about increasing capillary blood glucose testing and given parameters for when to call the provider. Abrupt withdrawal of the drug due to the topiramate component has been associated with seizures in clients without a history of seizures or epilepsy. In situations where immediate termination of phentermine plus topiramate is medically required, appropriate monitoring for seizure activity is recommended. Clients discontinuing the drug in a dosage of 15 mg/92 mg should be gradually tapered to reduce the possibility of precipitating a seizure.

Adverse effects of phendimetrazine that may occur include overstimulation of the body, which may result in

restlessness, nervousness, irritability, insomnia, headache, anxiety, tachycardia/palpitations, and difficulty concentrating.

Phendimetrazine is contraindicated with concurrent use of stimulant drugs such as benzphetamine, diethylpropion, and phentermine. It also is contraindicated in clients with hypersensitivity to the drug and other CNS stimulants. Other contraindications include advanced arteriosclerosis, symptomatic cardiovascular disease, moderate and severe hypertension, hyperthyroidism, and glaucoma. The drug should not be used for highly agitated or nervous clients or for clients with a history of substance misuse.

Benzphetamine is contraindicated in pregnant and lactating clients. It is also contraindicated in clients with known hypersensitivity to the drug and other sympathomimetics, advanced arteriosclerosis, or angle-closure glaucoma.

Table 32.2 is a drug prototype table for anorexiants featuring phentermine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anorexiant **Mechanism of Action** Causes CNS stimulation, specifically the release of norepinephrine from the hypothalamus, which in turn suppresses the appetite while increasing the basal metabolic rate, resulting in weight loss	**Drug Dosage** 15–37.5 mg orally every morning. *Lomaira only:* 8 mg 3 times daily. Administer 30 minutes before meals or 1–2 hours after meals.
Indications For adults with obesity as evidenced by a BMI ≥30 For overweight adults with a BMI of 27–29 and with one or more comorbidities of hypertension, type 2 diabetes mellitus, or dyslipidemia For children age 12+ with a BMI in the 95th percentile on growth charts **Therapeutic Effects** Reduces overall weight Increases metabolism	**Drug Interactions** MAOIs Tricyclic antidepressants (TCAs) Guanethidine Kratom (an herbal supplement) **Food Interactions** No significant interactions
Adverse Effects Palpitations/tachycardia Hypertension Ischemia Restlessness Dizziness Insomnia Dry mouth Altered taste Constipation Stomach pain Decreased libido Impotence	**Contraindications** Hypersensitivity to sympathetic amines Glaucoma (increased intraocular pressure) Hypertension (moderate-severe) History of cardiovascular disease MAOIs within 14 days (risk of hypertensive crisis) Pregnancy/lactation (teratogenic/fatal fetal effects) Caution: Hypertension Seizures Diabetes mellitus Children under age 16

TABLE 32.2 **Drug Prototype Table: Phentermine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking anorexiants:

- Assess the client's response to anorectic effects and dependency. It may become mentally and physically habit-forming (Mayo Clinic, 2023b).
- Monitor the client's cardiovascular status frequently because stimulant effects may alter blood pressure, heart

rate, exercise tolerance, and energy levels.
- Monitor for peripheral edema if the client's cardiovascular system is compromised and pulmonary hypertension develops.
- Monitor weight status at least three times per week.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an anorexiant should:

- Immediately report shortness of breath, chest pain, dizziness, fainting, or swelling of the extremities.
- Understand that within a few weeks, tolerance to the appetite-suppressant effects may develop. The client should not increase the dose. If this occurs, they should notify the prescriber.
- Monitor weight status at least three times per week, preferably at the same time of the day with the same amount of clothing using the same scale.
- Notify the provider of any sudden behavior or mood changes, such as mood swings and/or aggressive/angry outbursts.
- Take a missed dose as soon as possible; however, if it is close to the next dosage time, they should wait and just take the next dose.
- Be aware of the potential for misuse of the drug and that the drug can be habit-forming.

The client taking an anorexiant *should not:*

- Take stimulants at night because the stimulation effects may cause severe insomnia.
- Chew, crush, or open ER or SR capsules.
- Take double the dosage.

LINK TO LEARNING

National Institutes of Health Office of Dietary Supplements (https://openstax.org/r/factsweight)

Many clients do not consult their health care provider when choosing to use dietary supplements for weight loss. It is imperative that health care professionals become educated on the dietary supplements that clients may use to lose weight. The National Institutes of Health (NIH) has developed a comprehensive fact sheet for health care professionals on dietary supplements. The NIH also has a fact sheet for consumers on dietary supplements that health care professionals may find helpful in client education on the use of weight-loss supplements.

SAFETY ALERT

Anorexiants

Clients with an eating disorder who are taking anorexiants have an increased risk of developing dependency. Also, stimulation effects on the body may lead to critical or fatal cardiovascular effects.

32.3 Lipase Inhibitors

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 32.3.1 Identify the characteristics of lipase inhibitor drugs used for weight management.
- 32.3.2 Explain the indications, actions, adverse reactions, and interactions of lipase inhibitor drugs used for weight management.
- 32.3.3 Describe nursing implications of lipase inhibitor drugs used for weight management.
- 32.3.4 Explain the client education related to lipase inhibitor drugs used for weight management.

Lipase is a digestive enzyme that enables the body to digest and systemically absorb dietary fat. **Lipase inhibitors** bind to gastric and pancreatic lipases in the intestine. This prevents hydrolysis of dietary triglycerides into monoglycerides and fatty acids and the absorption of dietary fat. Currently, orlistat is the only one drug approved by the FDA as a lipase inhibitor (Yip & Ambizas, 2019).

Orlistat

Orlistat (Alli, Xenical) is a nonsystemic gastric lipase inhibitor that reduces intestinal absorption of dietary fat by approximately 30%. Orlistat binds to lipases, reducing absorption of dietary fat while also demonstrating the ability to lower total cholesterol, low-density lipoproteins, fasting glucose, and insulin concentrations. Additionally, client blood pressure measurements often improve (Sahebkar et al., 2018).

Orlistat is available as an oral capsule. Alli is available over the counter, whereas Xenical is available through a prescription. Capsules are taken up to three times a day, up to 1 hour before meals containing fat. Dietary fat is not absorbed systemically and is eliminated in feces.

Adverse Effects and Contraindications

Orlistat is not systemically absorbed, so the most common side effects are gastrointestinal: flatus, abdominal pain/discomfort, nausea, oily rectal discharge, fecal urgency, diarrhea, and fatty/oily stool. The adverse GI effects often subside within 4 weeks.

Orlistat is contraindicated in clients with hypersensitivity to the drug. It is also contraindicated in conditions such as gallbladder disease, cholestasis, malabsorption X drug syndrome, hypothyroidism, anorexia/bulimia nervosa, and organic causes of obesity. Orlistat is contraindicated in pregnant clients. It should be used cautiously with gastrointestinal diseases, nephrolithiasis, hyperoxaluria, and known dietary deficiencies of vitamins A, D, E, and K. Providers should exercise caution in older adults, lactating clients, and children under age 12.

Table 32.3 is a drug prototype table for lipase inhibitors featuring orlistat. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Lipase inhibitor **Mechanism of Action** Reduces pancreatic and gastric lipase, thereby reducing absorption of fat in the GI system	**Drug Dosage** One 120 mg capsule with each fat-containing meal (3 times per day).
Indications Overweight and obesity **Therapeutic Effects** Reduces overall weight Reduces GI absorption of dietary fat	**Drug Interactions** Pravastatin Vitamins A, D, E, and K HIV medications
Adverse Effects Flatus Oily rectal discharge Fecal urgency Fatty stool Headache	**Contraindications** Hypersensitivity to drug Malabsorption syndrome Cholecystitis Gallbladder disease Pregnancy Caution: GI disorders Vitamin deficiencies, especially A, D, E, and K Children under age 12

TABLE 32.3 **Drug Prototype Table: Orlistat** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking orlistat:

- Consistently monitor the client's weight, blood pressure, and serum lab values associated with obesity (e.g., lipids, glucose, and hepatic function tests).
- Monitor clients with diabetes closely for hypoglycemia and/or the need for medication reduction or elimination. With weight loss, a client's need for medications to treat diabetes may be reduced or eliminated.
- Monitor clients with hypertension closely. With weight loss, a client's need for medications to treat hypertension may be reduced or eliminated.
- Monitor client's weight every 3 months for dosage changes as needed.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking orlistat should:

- Distribute daily fat intake evenly across all three meals.
- Be educated to supplement with a multivitamin that also contains vitamins A, D, E, and K because lipase inhibitors may prevent absorption of fat-soluble vitamins. Vitamin supplements should be taken 2 hours before or after taking a lipase inhibitor.
- If taking levothyroxine concurrently, take orlistat 4 hours before or 4 hours after levothyroxine to avoid reducing the serum availability of levothyroxine.
- Report low blood glucose levels to their health care provider because their medication may need to be readjusted or eliminated with weight loss.

The client taking orlistat *should not:*

- Eat very high-fat meals, to minimize uncomfortable GI effects.

Nonpharmacological Lipase Inhibitors

Nonpharmacological natural lipase inhibitors are present in various foods and supplements. Ox bile supplements have lipase inhibitor activity and are taken in much the same way as orlistat. Although ox bile supplements are considered safe, they may cause uncomfortable GI symptoms and deficiencies in fat-soluble vitamins (A, D, E, K). Ox bile supplements have been used for centuries in Eastern medicine to support various GI symptoms.

Less-invasive natural lipase inhibitors include caffeine, green coffee bean extract, tea (especially green tea), panax ginseng, soybeans, apples, grapevines, yerba mate, mulberry extract, and peanuts. These food items and supplements may contain several natural lipase inhibitors such as flavonoids, lactones, and polyphenols. However, any weight-loss supplements should only be used under the guidance of a weight-management health care professional.

SPECIAL CONSIDERATIONS

Losing Weight

Finding a health care professional with experience in weight loss improves a person's long-term weight-loss and management success. Different modalities work for different clients. An experienced weight-loss health care professional can develop an individualized weight-loss plan that includes a foundation of meal planning and exercise.

(Source: Perrault, 2022)

32.4 Other Drugs, Supplements, and Herbal Remedies

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 32.4.1 Identify the characteristics of miscellaneous drugs and herbal supplements used for weight management.
- 32.4.2 Explain the indications, actions, adverse reactions, and interactions of miscellaneous drugs and herbal supplements used for weight management.
- 32.4.3 Describe nursing implications of miscellaneous drugs and herbal supplements used for weight management.
- 32.4.4 Explain the client education related to miscellaneous drugs and herbal supplements used for weight management.

Obesity is a global concern that may not be managed by diet and exercise alone. There are other adjunct medications and supplements that can promote weight loss in conjunction with diet and exercise.

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

GLP-1 receptor agonist medications were originally developed to treat type 2 diabetes and control blood sugar; however, they have been found to also cause weight loss and decrease the risk of cardiovascular events such as heart attacks and strokes in clients with diabetes.

Semaglutide

Semaglutide, which mimics the GLP-1 hormone that is released in the gut in response to eating, is the newest medication for weight management. Semaglutide is approved for weight loss only under the brand name Wegovy. Semaglutide is also the active ingredient in several medications used to treat diabetes (Ozempic, Rybelsus). However, due to differing doses and differences in how the drug is packaged, prescribers should take caution when prescribing off-label.

Semaglutide is intended for use in adults with an initial BMI of 30 kg/m^2 or greater (obesity) or an initial BMI of 27 kg/m^2 or greater (overweight) and at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, or dyslipidemia (DailyMed, *Wegovy*, 2023). Semaglutide may be used in pediatric clients over age 12 who have an initial BMI at or above the 95th percentile for their age and sex. According to UCLA Health (2023), semaglutide emphasizes treating obesity as a chronic metabolic disease rather than solely a condition that requires lifestyle/behavioral changes.

TRENDING TODAY

Weight Loss Benefits with Semaglutide

Losing weight can positively affect many body systems, especially the cardiovascular system; however, semaglutide itself may also have cardiovascular benefits. A report by NBC News (https://openstax.org/r/nbcnews) discusses a potential reduction of cardioembolic events such as a myocardial infarction or cerebrovascular accident (stroke) in clients taking semaglutide.

When the blood glucose levels rise in response to ingested food, semaglutide mimics the GLP-1 hormone to stimulate insulin release and decrease glucagon release. This action lowers serum glucose levels and delays gastric emptying. A decrease in blood glucose and delayed gastric emptying suppress the appetite, which aids in weight loss. Note that because semaglutide delays gastric emptying, it may alter the absorption of other medications and supplements.

Liraglutide

Liraglutide has been shown to be an effective treatment to reduce weight in clients with obesity. Liraglutide is an injectable medication classified as a glucagon-like peptide receptor agonist and incretin mimetic that triggers increased insulin release and decreased glucagon release, lowering post-prandial blood glucose levels. By causing a glucose-dependent release of insulin and a decrease in blood glucagon levels, there is a delay in gastric emptying, leading to appetite suppression and weight loss. This action also causes an ancillary increase in heart rate of 10–20

beats per minute above the client's baseline.

Liraglutide is highly bound to protein, has a large distribution area, and has a half-life of approximately 13 hours. This allows for a once-a-day subcutaneous (SQ) injection (abdomen, thigh, upper arm) without regard to meals to be effective. Double gloves and a protective gown (and goggles if necessary) should be worn during preparation and SQ administration to avoid unintentional absorption through the skin. Liraglutide has caused thyroid C-cell tumors in mice (DailyMed, *Saxenda,* 2021).

Table 32.4 lists common GLP-1 drugs for weight loss and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Semaglutide (Wegovy)	*Initial dose:* 0.25 mg subcutaneously once a week for 4 weeks. *Weeks 5–8:* 0.5 mg/week. *Weeks 9–12:* 1 mg/week. *Weeks 13–16:* 1.7 mg/week. *Weeks 17 and onward:* 1.7 mg or 2.4 mg/week. *Maximum dose:* 2.4 mg/week.
Liraglutide (Saxenda)	*3 mL prefilled injection pen:* 6 mg/mL. Initial dose: 0.6 mg/day subcutaneously. After 1 week, increase daily dose by 0.6 mg per week at weekly intervals to reach 3.0 mg. Maximum dose: 3.0 mg/day.

TABLE 32.4 **Drug Emphasis Table: GLP-1 Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Both semaglutide and liraglutide are contraindicated in clients with a personal or family history of medullary thyroid carcinoma (MTC), multiple endocrine neoplasia syndrome type 2 (MEN 2), serious hypersensitivity to liraglutide, diabetic ketoacidosis (DKA), pancreatitis, suicidal attempts/ideation, pregnancy, and lactation. Semaglutide and liraglutide should be used cautiously in clients with alcohol use disorder, severe hypoglycemia, gastroparesis, renal and/or hepatic impairment, or history of angioedema. Caution should be exercised when used concurrently with insulin and insulin secretagogues like sulfonylureas. They should also be used cautiously in older adults. Safety in children under age 10 has not been established.

Table 32.5 is a drug prototype table for GLP-1 receptor agonists featuring semaglutide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class GLP-1 receptor agonist; incretin mimetic **Mechanism of Action** Stimulates insulin release in the body while decreasing the release of glucagon, delaying gastric emptying and lowering postprandial serum glucose levels	**Drug Dosage** *Initial dose:* 0.25 mg subcutaneously once a week for 4 weeks. *Weeks 5–8:* 0.5 mg/week. *Weeks 9–12:* 1 mg/week. *Weeks 13–16:* 1.7 mg/week. *Weeks 17 and onward:* 1.7 mg or 2.4 mg/week. *Maximum dose:* 2.4 mg/week.
Indications Adjunct therapy along with reduced-calorie diet and increased physical activity in weight management for adults with obesity or overweight and at least one weight-related comorbidity In pediatric clients age 12 or older with an initial BMI ≥95th percentile for their age and sex **Therapeutic Effects** Weight loss	**Drug Interactions** Sulfonylurea Insulin **Food Interactions** No significant interactions
Adverse Effects Acute pancreatitis Acute gallbladder disease Hypoglycemia Acute kidney injury Tachycardia/palpitations Suicidal behavior and ideation Nausea and/or vomiting Diarrhea Abdominal pain Flatulence Gastroparesis	**Contraindications** Personal/family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2 Prior hypersensitivity to the drug or other GLP-1 receptor agonist

TABLE 32.5 **Drug Prototype Table: Semaglutide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking GLP-1 receptor antagonist drugs:

- Consistently monitor the client's weight, blood pressure, and serum lab values associated with obesity (e.g., lipids, glucose, and hepatic function tests).
- Monitor clients with diabetes closely for hypoglycemia and/or the need for medication reduction or elimination. With weight loss, a client's need for medications to treat diabetes may be reduced or eliminated.
- Teach clients to monitor for signs and symptoms of hypoglycemia that may occur from weight loss and/or the supplement such as headache, nervousness, irritability, sweating, clammy skin, shakiness, and palpitations.
- Monitor client's weight every 3 months for dosage changes as needed.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a GLP-1 receptor antagonist should:

- Use proper SQ injection technique and rotate injection sites weekly (liraglutide).
- Monitor capillary blood glucose levels closely; immediately report hypoglycemia to the provider.
- Drink adequate fluids to ensure hydration.

- Avoid alcohol, which may interfere with weight-loss drugs and potentially cause hypoglycemia.
- Maintain an accurate food log that includes ingestion of water and physical activity. Handwritten logs facilitate clients staying on track and achieving success. Some clients use smartphone apps to log meals, water intake, and physical activity.
- Follow up with their provider as instructed.

FDA BLACK BOX WARNING

Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Semaglutide and **liraglutide** have been associated with thyroid tumors in animal studies; relevance to humans has not been established.

Other Drugs for Weight Management

Additional adjunct drugs and supplements target enzymatic and lipid metabolism to manage chronic obesity. These drugs do not fit into the previous categories of pharmacotherapeutics.

Bupropion Naltrexone

Bupropion naltrexone (Contrave) is a combination of an antidepressant (bupropion) and an opioid antagonist (naltrexone). Bupropion is commonly used for adult depression, seasonal affective disorder (SAD), and smoking cessation. Naltrexone is commonly used for substance use disorders because it blocks opioid receptors and the euphoric effects of alcohol and opioids. In combination, these two drugs have been found to promote weight loss as a dopamine reuptake inhibitor by affecting two different areas of the brain involved in hunger and satiety stimuli—the hypothalamic appetite regulatory center and the mesolimbic dopamine circuit reward system. The resultant decreased appetite results in therapeutic weight loss.

Bupropion naltrexone is indicated for chronically overweight clients or those with chronic obesity with at least one other comorbidity (hypertension, type 2 diabetes, or dyslipidemia). This drug is used as an adjunct to a low-calorie diet and increased exercise in clients with obesity. Both drugs are well-absorbed orally, and a low-fat meal enhances absorption.

Adverse Effects and Contraindications

Adverse effects of bupropion naltrexone include life-threatening anaphylactic reactions (pruritis, urticaria, hives, dyspnea, angioedema), homicidal/suicidal thoughts and behaviors, and seizures. Common adverse effects include nausea, vomiting, constipation, and headache. Clients should be instructed to contact their provider immediately if any abnormal symptoms occur. Clients with diabetes should monitor capillary blood glucose levels 3–4 times per day for hypoglycemia caused by the drug and/or weight loss.

Contraindications include a known hypersensitivity to bupropion or naltrexone, uncontrolled hypertension, end-stage renal disease, severe hepatic impairment and concurrent use of CYP2B6 inducers, seizure disorders, anorexia or bulimia, pregnancy, and in children. Concurrent use is contraindicated within 14 days of the use of an MAOI or use of opioids or other bupropion medications and antidepressants including selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (TCAs). Bupropion naltrexone should be used cautiously in older adults secondary to possible adverse CNS effects and decreased renal excretion. Dosages are often decreased in cases of renal and hepatic impairment. Use of other bupropion-containing products may increase the risk of seizures. Bulimia and anorexia nervosa may also increase the risk of seizures.

Table 32.6 is a drug prototype table for other weight-loss drugs featuring bupropion naltrexone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Dopamine and norepinephrine reuptake inhibitor and opioid antagonist **Mechanism of Action** Stimulates and inhibits various pathways of the central nervous system (CNS), resulting in weight reduction and maintenance of weight loss	**Drug Dosage** *Extended-release tablet, bupropion 90 mg/naltrexone 8 mg:* *Initial dose:* 1 tablet in the morning for 1 week. *Week 2:* 1 tablet in the morning and 1 tablet in the evening. *Week 3:* 2 tablets in the morning and 1 tablet in the evening. *Week 4+:* 2 tablets in the morning and 2 tablets in the evening. Onset: within 4 weeks; peak: 6 months. Maximum dose: 32 mg naltrexone/360 mg bupropion orally daily.
Indications Weight loss and maintenance **Therapeutic Effects** Weight loss	**Drug Interactions** MAOIs Drugs metabolized by CYP2D6 Digoxin Concomitant use with CYP2B6 inhibitors CYP2B6 inducers Dopaminergic drugs **Food Interactions** No significant interaction
Adverse Effects Nausea/vomiting Constipation/diarrhea Headache Dizziness Insomnia Dry mouth	**Contraindications** Uncontrolled hypertension Seizure disorder Anorexia nervosa or bulimia Clients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs Use of other bupropion-containing products Chronic opioid use During or within 14 days of taking an MAOI Known allergy to any ingredients

TABLE 32.6 **Drug Prototype Table: Bupropion Naltrexone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking bupropion naltrexone:

- Consistently monitor the client's weight, blood pressure, and serum lab values associated with obesity (e.g., lipids, glucose, and hepatic function tests).
- Monitor clients with hypertension closely. With weight loss, a client's need for medications to treat hypertension may be reduced or eliminated.
- Monitor client's weight every 3 months for dosage changes as needed.
- Monitor for worsening signs of depression or suicidal ideation that may occur with some weight-loss supplements. It is critical that clinicians assess clients' mental status, mood changes, and significantly increased signs of depression (depressed mood, loss of interest in usual activities, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, irritability, hostility, suicide attempt, or suicidal ideation), especially during the initial few months of therapy.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking bupropion naltrexone should:

- Immediately report any increase in depressive symptoms and/or suicidal ideation to provider.
- Report any signs or symptoms, such as headache, palpitations, dizziness, nervousness, irritability, to the provider.
- Drink adequate fluids to ensure hydration.
- Avoid alcohol, which may interfere with weight-loss drugs and potentially cause hypoglycemia.
- Maintain an accurate food log that includes ingestion of water and physical activity. Handwritten logs facilitate clients staying on track and achieving success. Some clients use smartphone apps to log meals, water intake, and physical activity.
- Follow up with their provider as instructed.

FDA BLACK BOX WARNING

Bupropion

Bupropion has been shown to increase the risk of suicidal thoughts and behavior in short-term trials.

Supplements and Herbal Remedies for Weight Management

Supplements such as chromium picolinate, conjugate linoleic acid, glucomannan, green tea extract, guarana, and hoodia have been credited with supporting weight loss. The success of these supplements, just like drugs, relies on their being adjuvant to low-calorie meals and exercise. A successful weight-management plan is individualized and client centered and may include natural food or herbal supplements to aid in weight loss. Stress-reduction techniques also play a role in lowering cortisol levels and improving mental well-being because stress may impede weight-loss success.

Chromium Picolinate

Chromium is an essential mineral involved in glucose metabolism and is often called glucose tolerance factor (GTF). It is found in various foods such as beef, chicken, eggs, dairy products, broccoli, potatoes, and garlic, but it is poorly absorbed, prompting some clients to use supplements. Picolinate acid, an amino acid, is added to chromium to improve the absorption and aid insulin function. However, excessive supplementation can lead to toxicity. Research indicates that chromium picolinate can lower blood glucose and serum cholesterol, promote fat loss, and increase lean muscle mass, especially in clients with type 2 diabetes. Clients who are dependent on insulin should use it under medical guidance and monitor their capillary blood glucose levels (Balch, 2023).

Conjugated Linoleic Acid

Conjugated linoleic acid (CLA) is a polyunsaturated fatty acid found naturally in animal food products such as beef, lamb, butter, and dairy products. Synthetic CLA may be produced from safflower, sunflower, corn, and soybean oils. This essential fatty acid has been found to have antiobesogenic and antiatherosclerotic properties (den Hartigh, 2019). The metabolic mechanism of action of CLA reduces lipogenesis while promoting lipolysis to improve body composition. Studies have found that CLA increases lipolysis significantly in human fat cells (adipocytes) while decreasing the synthesis of fatty acids (Basak & Duttaroy, 2020). The use of CLA may interfere with CYP enzyme functions. It may also interfere with the effectiveness of tamoxifen, a breast cancer medication.

Glucomannan

Processed foods have removed much of the natural fiber in the American diet. Fiber supplements are often used for overall health and wellness. Glucomannan is a dietary fiber extracted from the konjac (elephant yam), a Japanese root vegetable. Glucomannan passes unchanged into the colon, where it works as a dietary fiber. It is one of the most potent fibers because it can absorb up to 50 times its weight in water; therefore, a smaller amount is taken than for other fiber supplements.

Some research has shown that supplementing with glucomannan may reduce body weight but not BMI in the short

term in otherwise healthy adults with overweight or obesity. Other research has shown that daily 4-gram doses of glucomannan consumed over 8 weeks did not lead to weight loss or changes in body composition, did not lead to feelings of hunger or meal satiation, and did not impact cholesterol or blood sugar levels (MacPherson, 2022).

Glucomannan reduces weight in the same way as other water-soluble, fermentable fibers do—through low energy density and bulking properties causing a laxative effect. The absorption of water expands glucomannan in the gastrointestinal tract, producing satiety. Additionally, glucomannan, like all fiber foods, stabilizes blood glucose levels and reduces total cholesterol and LDL levels through fecal excretion. As with all fiber supplements, adequate water intake is essential to avoid constipation.

Green Tea Extract

Second to water, tea is the most consumed beverage globally. Green tea is one of the healthiest teas available for consumption. Green tea contains polyphenols and phytochemicals with antioxidant and antiviral properties. The health-enhancing properties of green tea are numerous. One of the polyphenols in green tea helps protect the DNA in the body's cells from oxidative stress. This boosts the body's immune system to combat many conditions and illnesses, including cancer. A study in South Korea found that consistently drinking green tea reduced abdominal obesity by 44% (Kwak & Shin, 2022).

The natural pharmacological effects of green tea are related to the increased fatty acid oxidation that reduces body and abdominal fat. Additionally, green tea lowers concentrations of total cholesterol, serum free fatty acids, and leptin levels. These effects may decrease the incidence of metabolic syndrome.

Guarana

Guarana is a seed with stimulant and phytochemical properties containing caffeine as the active ingredient. It is used as a general intestinal detoxification herb and stimulant to improve mental alertness and increase metabolic rate. Guarana is rich in antioxidants and is like green tea in its properties. Consumers can find guarana in energy drinks, soft drinks, smoking-cessation products, and vitamin supplements. Guarana alone does not significantly promote weight loss; it must be combined with a low-calorie diet and exercise. Due to the stimulant effects, guarana should not be used by clients with hypertension or cardiovascular conditions such as dysrhythmias. A disadvantage for consumers is that it is not easy to determine how much caffeine content any specific product contains.

Hoodia Gordonii

Hoodia gordonii, commonly called hoodia, is an African cactus that the San Bushmen used historically as an appetite suppressant. There are several hoodia supplements marketed as weight-loss supplements. According to the National Center for Complementary and Integrative Health (2020), there has been little research on the weight-loss properties of hoodia in humans and its efficacy in weight loss.

Nursing Implications

The nurse should do the following for clients who are taking supplements and herbal remedies for weight management:

- Teach clients to monitor for signs and symptoms of hypoglycemia that may occur from weight loss and/or the supplement. Signs of hypoglycemia include headache, nervousness, irritability, sweating, clammy skin, shakiness, and palpitations.
- Educate clients that some over-the-counter (OTC) products may not be safe and can interact with other prescribed medications, including increasing the risk of hypoglycemia. Recreational alcohol ingestion may also cause hypoglycemia.
- Monitor for worsening signs of depression or suicidal ideation that may occur with some weight-loss supplements. It is critical that clinicians assess clients' mental status, mood changes, and significantly increased signs of depression (depressed mood, loss of interest in usual activities, insomnia or hypersomnia, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, irritability, hostility, suicide attempt or suicidal ideation), especially during the initial few months of therapy.
- Provide client teaching regarding the supplement or herbal remedy and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a supplement or herbal remedy for weight management should:

- Maintain an accurate food log that includes ingestion of water and physical activity. Handwritten logs facilitate clients staying on track and achieving success. Some clients use smartphone apps to log meals, water intake, and physical activity.
- Incorporate healthy meal planning and physical activity in their overall weight-management plan.
- Learn about the safety and efficacy of products because they are not medically investigated or regulated.
- Talk with their health care provider for a fully informed weight-loss plan.
- Follow the manufacturer's and provider's guidelines.

The client taking a supplement or herbal remedy for weight management *should not:*

- Use weight-loss products without consulting a health care provider experienced in weight management. All supplements are not the same.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Ellen Normandy is a 58-year-old female client who has been "watching" her diet and exercising at the local fitness club for the past 12 months to lose weight. She has lost 6.7 pounds. Frustrated, she arrives at her health care provider's office to ask for medication. The provider takes vital signs and a fasting capillary blood glucose (CBG) level.

History
Laparoscopic cholecystectomy due to cholelithiasis
Laparoscopic total hysterectomy and oophorectomy
Mild hyperlipidemia

Current Medications
Multivitamin daily

Vital Signs		Physical Examination
Temperature:	97.9°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; no peripheral edema bilaterally; S1, S2 noted; no extra sounds or murmurs • *Respiratory:* Lungs clear upon auscultation to all fields; no use of accessory muscles • *GI:* Abdomen soft, nontender, slightly distended, obese • *GU:* Reports normal urine output—every 2–4 hours based on water intake; complains of constipation; last bowel movement 3 days ago • *Neurological:* Within normal limits • *Integumentary:* No wounds noted; skin appropriate for age
Blood pressure:	148/96 mm Hg	
Heart rate:	88 beats/min, regular	
Respiratory rate:	16 breaths/min, regular	
Oxygen saturation:	99% on room air	
Height:	5'9"	
Weight:	278 lb	
BMI:	41.1 kg/m^2	
CBG:	157 mg/dL	

TABLE 32.7

1. Based on the information above, the nurse anticipates which primary medical diagnosis by the health care provider?
    a. Type 2 diabetes mellitus
    b. Metabolic syndrome
    c. Overweight
    d. Obesity

2. Which of the following indicates Ellen's BMI classification?
    a. Overweight
    b. Class I obesity
    c. Class II obesity
    d. Class III obesity

Chapter Summary

This chapter discussed the differences between overweight and obesity and their pathophysiology. Clinical manifestations were also explained. A variety of pharmacological methods of weight management were discussed, including anorexiants, lipase inhibitors, and other drugs. The chapter also described various supplements and herbal remedies for weight loss.

Despite the availability of OTC and prescribed weight-loss drugs and supplements, the chapter discussed how the best strategy for weight loss is lifestyle modifications, such as exercise and caloric restriction, as a proven effective treatment in obesity. However, lifestyle modifications do not always promote optimal weight loss. Often supplements and/or medications are required. Once a healthy weight is achieved, clients must continue to practice healthy habits to maintain weight management.

Key Terms

adipose pertaining to fat; fatty

body mass index (BMI) an index for estimating obesity obtained by dividing the weight in pounds/kilograms by height in inches/meters squared, following a formula

cholelithiasis the presence or formation of gallstones

circadian rhythm diverse yet predictable changes in physiological variables, including sleep, appetite, temperature, and hormone secretion, over a 24-hour period

clean eating eating foods that are in their natural state with no chemical additives or preservatives

food desert an area where the population/community has extremely limited access to healthy, affordable food

ghrelin a polypeptide secreted by the stomach that increases appetite, participates in energy homeostasis, and regulates body weight

glucagon a polypeptide hormone secreted by the alpha cells of the pancreas that increases the blood glucose level by stimulating the liver to change stored glycogen to glucose (gluconeogenesis); glucagon opposes the action of insulin and can be administered as an injection to reverse hypoglycemia

glycemic index (GI) a value between 0 and 100 that measures how a specific food increases the blood level of glucose. A score at the low end of the scale (less than 55) indicates a low glycemic index food that has a slow or minimal effect on the blood glucose level; this provides consistency in blood glucose levels.

hyperplasia an abnormal increase in the number of normal cells in an organ or tissue with no evidence of cancer

hypertrophy an increase in the size of an organ, structure, or cellular component of the body

insulin a hormone secreted by the beta cells of the pancreas; a drug principally used to control diabetes mellitus

insulin resistance a missing or lack of response of the muscle, fat, or liver cells to insulin that results in impaired glucose metabolism; also known as insulin sensitivity

leptin a helical peptide hormone produced by adipose tissue that acts on cells in the hypothalamus to suppress appetite and increase metabolism in response to increases in body fat storage; also involved in the onset of puberty and pancreatic insulin secretion

leptin resistance a decrease in the ability of leptin to suppress appetite or increase the body's energy use

lipase an enzyme that breaks down ingested fat into fatty acids in the GI tract

lipase inhibitor substances used to reduce the activity of lipases found in the GI tract

Mediterranean diet a well-tolerated, palatable diet modeled on the traditional cuisines of Italy, Greece, and the islands of the Mediterranean Sea that includes fish/seafood, wine, whole vegetables, nuts, seeds, and olive oil, deriving 25%–35% of calories from fat

metabolic syndrome the presence of three or more interrelated atherosclerotic risk factors: insulin resistance, elevated fasting blood glucose, hypertension, elevated triglycerides, reduced high-density lipoproteins, abdominal obesity, or increased waist circumference

nutrient-dense foods foods rich in vitamins and minerals vital for health without saturated fats, sugars, and sodium

obesity a body mass index of 30 kg/m^2 or higher; an unhealthy accumulation of body fat

obesity hypoventilation syndrome a respiratory consequence of obesity that is characterized by alveolar hypoventilation during sleep and wakefulness.

overweight a body mass index between 26 and 29 kg/m^2; having a weight higher than what is expected for a person's age, sex, height, and build

serotonin deficiency a lack of serotonin, a neurotransmitter and vasoconstrictor with a vital role in cellular processes of sleep–wake cycles, intestinal motility, nausea, vomiting, obsessive-compulsive disorder (OCD), depression, and eating; deficiency may play a role in increasing depression, anxiety, mania, and other health conditions, including weight gain

sleep apnea the temporary cessation of breathing during sleep

steatosis fatty degeneration

thermogenesis the production of heat by the mitochondria within the cells that burn calories and adipose tissue

thermogenic foods foods that if eaten cause a rise in the production of body heat (burns calories and adipose tissue)

weight bias negative attitudes, beliefs, judgements, stereotypes, and discriminatory acts aimed at individuals because of their weight

weight stigma the negative stereotyping of people with overweight or obesity as lacking self-discipline, being lazy or sloppy, and lacking intelligence

Review Questions

1. A nurse is presenting a workshop on weight management. The nurse explains overweight and obesity are determined by:
   a. Weight in pounds
   b. Height in centimeters
   c. Genetics
   d. Body mass index (BMI)

2. A nurse performs an initial assessment of a client with a height of 5’9” and a weight of 278 pounds. What BMI does the nurse calculate for this client?
   a. 51.2 kg/m^2
   b. 41.1 kg/m^2
   c. 31.2 kg/m^2
   d. 21.1 kg/m^2

3. A nurse is providing education to a group of adults about the differences between overweight and obesity. Which statement by one of the participants demonstrates an accurate understanding of these terms?
   a. “Overweight and obesity are essentially the same, just different terms for having excess body fat.”
   b. “Overweight refers to having a BMI between 25 and 29.9, whereas obesity is defined as a BMI of 30 or higher.”
   c. “Obesity is a medical condition, whereas overweight is merely a cosmetic concern.”
   d. “Being overweight is a more severe health condition than obesity due to the increased risk of cardiovascular diseases.”

4. The clinic nurse is teaching a 25-year-old female client about her new prescription for benzphetamine. What statement by the client indicates understanding?
   a. “It is best to use a method of birth control because the medication can be harmful to a fetus.”
   b. “This medication will make me very sleepy.”
   c. “I will be hungry on this medication.”
   d. “This medication is best taken right before bed.”

5. A provider at a weight-loss clinic is considering starting phentermine for a 35-year-old client. The nurse is performing a medication reconciliation for the client. Which medication would the nurse have concerns about?
   a. Acetaminophen
   b. Omeprazole
   c. Zinc
   d. Phenelzine

6. While counseling a client on different anorexiants, the nurse advises them that office visits may be required

every 14 days to assess progress and evaluate the effectiveness of the weight-loss medication. The nurse is referring to which medication?

a. Phentermine
b. Phendimetrazine
c. Phentermine/topiramate
d. Benzphetamine

7. The nurse is aware that which lipase inhibitor is available by prescription from a provider and also over the counter at a lower dose?

a. Orlistat
b. Phentermine
c. Bupropion naltrexone
d. Benzphetamine

8. The nurse is providing client education on the drug orlistat. The nurse explains common adverse effects of orlistat that subside within 4 weeks are:

a. Palpitations (tachycardia)
b. Headache and dizziness
c. Diarrhea and fatty stool (steatorrhea)
d. Itchiness and high blood pressure

9. The nurse is aware that a combination medication of an antidepressant and an opioid antagonist may be prescribed for weight loss. Which medication is it?

a. Chromium picolinate and naltrexone
b. Phentermine and topiramate
c. Phenelzine and naloxone
d. Bupropion and naltrexone

10. A nurse is providing education to a client who has been prescribed orlistat (Alli) for weight loss. The client asks the nurse how this medication works to help with weight loss. Which response by the nurse is most accurate?

a. “Orlistat suppresses appetite, making you feel less hungry and eat fewer calories.”
b. “This medication increases your metabolism, helping you burn more calories.”
c. “Orlistat blocks the absorption of dietary fat, reducing calorie intake from fat and promoting weight loss.”
d. “It works by reducing water retention in the body, leading to weight loss.”

CHAPTER 33
Introduction to the Renal and Urinary Systems

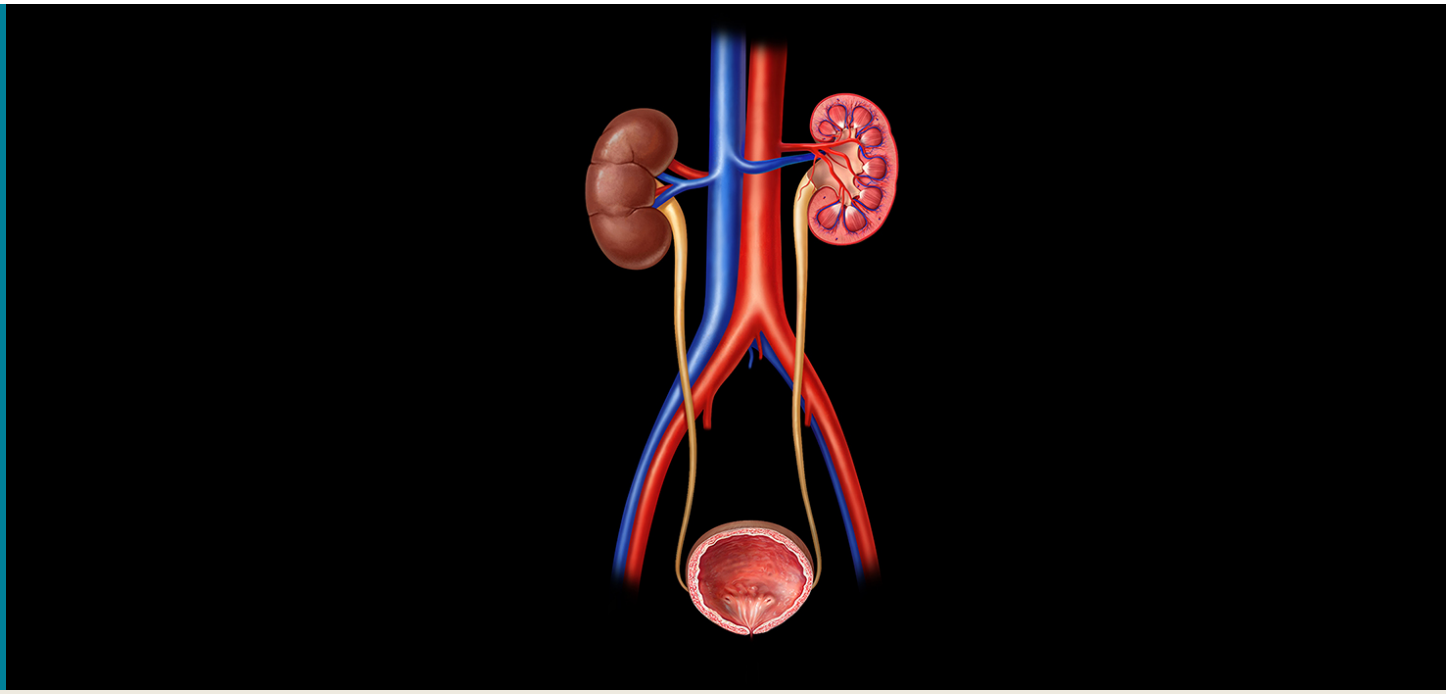


FIGURE 33.1 The renal and urinary system filters out excess fluid and eliminates urea from the body, helping body chemicals stay in balance. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The renal system, consisting of the kidneys, ureters, and urethra, has several essential functions (Ogobuiro & Tuma, 2022). In addition to filtering and removing waste products from the body, it also regulates plasma osmolarity, acid-base balance, and blood pressure (BP). Accordingly, the renal system affects many cells and organs within the body. Acute kidney injury affects as many as 60% of all critically ill hospitalized clients (Pickkers et al., 2021). The ureters, bladder, and urethra are at risk from infection, obstruction, vascular compromise, and other conditions. Chronic renal disease, often associated with hypertension and diabetes, affects one in seven adults, and 90% of those affected are unaware of their condition (National Institute of Diabetes and Digestive and Kidney Diseases, 2021).

33.1 Introduction to the Renal System

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 33.1.1 Describe the structure and function of the renal system.
- 33.1.2 Name common conditions that affect the renal system.

Kidneys

The kidneys have three main functions: filtration, reabsorption, and secretion. The kidneys filter 200 liters of fluid daily to remove waste products that exit the body in the urine. Collecting important nutrients, ions, and proteins protects the body against deficiencies. The individual processes for the three main functions are listed here and

explained in greater detail in later sections of this chapter:

- Removal of the waste products of metabolism
- Regulation of electrolytes and fluid
- Acid–base balance regulation
- Maintenance of systemic blood pressure
- Erythropoietin secretion
- Vitamin D_3 metabolism
- Gluconeogenesis

Kidneys' Anatomical Structure

The kidneys are two bean-shaped organs positioned in the retroperitoneum slightly above the waist, between the T12 and L3 vertebrae. The right kidney sits slightly lower than the left to accommodate the liver. Each kidney weighs approximately 135–150 g and is approximately 10–12 cm long. The adrenal glands are located on the upper pole of each kidney, and the spleen is connected anteriorly to the upper pole of the left kidney by the splenorenal ligaments.

The exterior of the kidney has three protective layers: the renal fascia, which is the outermost layer; the perirenal fat capsule; and the renal capsule, which consists of fibrous connective tissue. The interior of the kidney is divided into three distinct areas: the outermost cortex, the medulla, and the renal pelvis. The **renal cortex** contains **nephrons**, the functional units of the kidney, which merge into the collecting ducts and the convoluted tubules. The **renal medulla** contains 8 to 18 renal pyramids with the bases located adjacent to the cortex and the apices connecting to the minor calyces (Sorano et al., 2023). The minor calyces drain into the major calyces, which are large collecting spaces near the ureters' superior edge. The renal papillae are openings at the bottom of the renal pyramids where urine enters the collecting ducts. The renal columns are cortical tissues that separate the pyramids and provide space for the interlobar arteries. The urine moves from the pyramids to the funnel-shaped **renal pelvis** in the center of the kidney to the ureters (see Figure 33.2).

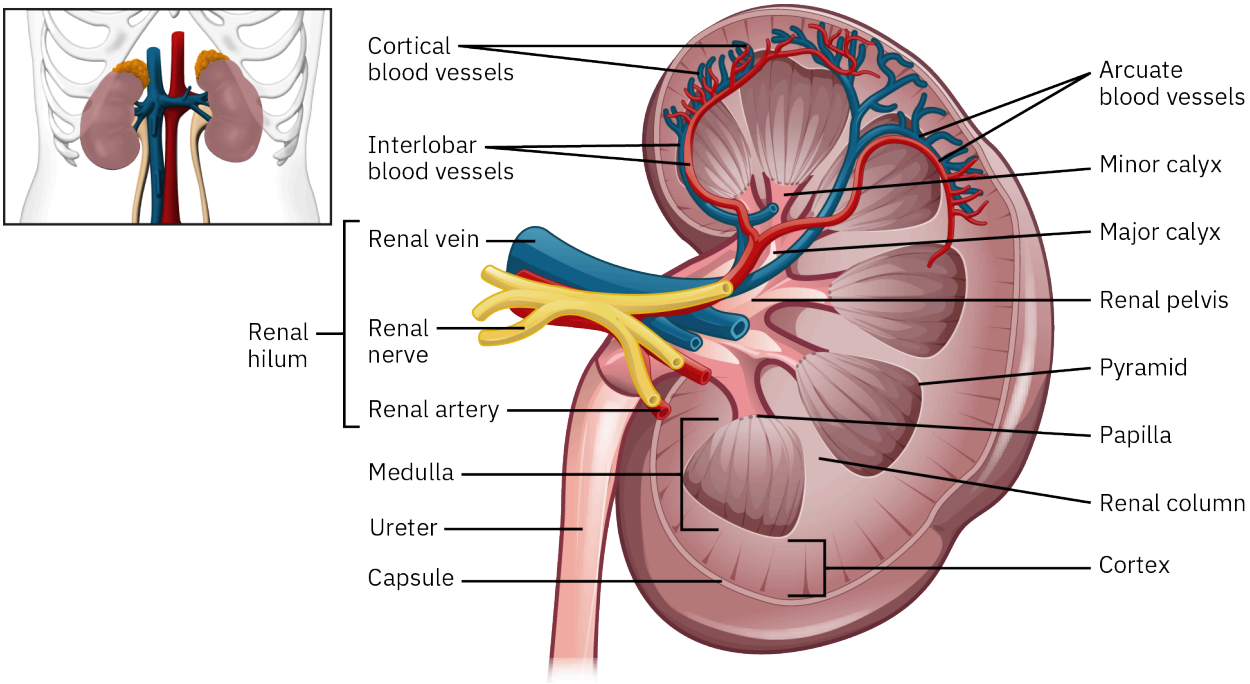


FIGURE 33.2 The renal columns serve to divide the kidney into 6–8 lobes and provide a supportive framework for vessels that enter and exit the cortex. The pyramids and renal columns taken together constitute the kidney lobes. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Kidneys' Vascular Structure

The renal arteries branch off the aorta at the L1/L2 intervertebral disk level just inferior to the mesenteric artery. Each artery is 4–6 cm long and 5–6 mm in diameter. The renal artery divides into anterior and posterior branches before entering the kidney at the **hilum**, an indentation on the medial side of the organ that allows blood vessels,

lymphatic vessels, and nerves to enter and exit the kidney. The segmental arteries eventually form the arterioles that supply the glomerular capillaries. The **vasa recta** is the network of capillaries that supply the proximal and distal tubules and the **loop of Henle**.

Kidneys' Lymphatic Structure

Two separate lymphatic systems supply the kidney. One branch supplies the interior and the exterior of the renal capsule in the cortex, and the other surrounds the arterial blood vessels. Both systems drain from the hilum into the para-aortic lymph nodes.

Kidneys' Neural Structure

The sympathetic division of the autonomic nervous system innervates the kidney. The splanchnic nerves from the renal plexus control the constriction of the arterioles in the renal cortex. These nerves travel from the renal vessels to the smooth muscle of the remaining areas of the nephron, including the juxtaglomerular cells that secrete renin. Sympathetic stimulation results in constriction of the renal vessels and the release of renin. In addition, there are pain receptors in the renal and urinary structures from the renal pelvis to the urinary meatus.

LINK TO LEARNING

Kidney Function

Access multimedia content (https://openstax.org/books/pharmacology/pages/33-1-introduction-to-the-renal-system)

This National Kidney Foundation video provides a brief overview of kidney function and kidney disease.

Nephrons

The nephron is the functional unit of the kidney and contains these structures (see Figure 33.3):

- Glomerulus and Bowman's capsule, which together comprise the renal corpuscle
- Proximal convoluted tubule, located in the renal cortex
- Descending loop of Henle
- Ascending limb in the renal medulla
- Thick ascending limb
- Distal convoluted tubule
- Collecting duct

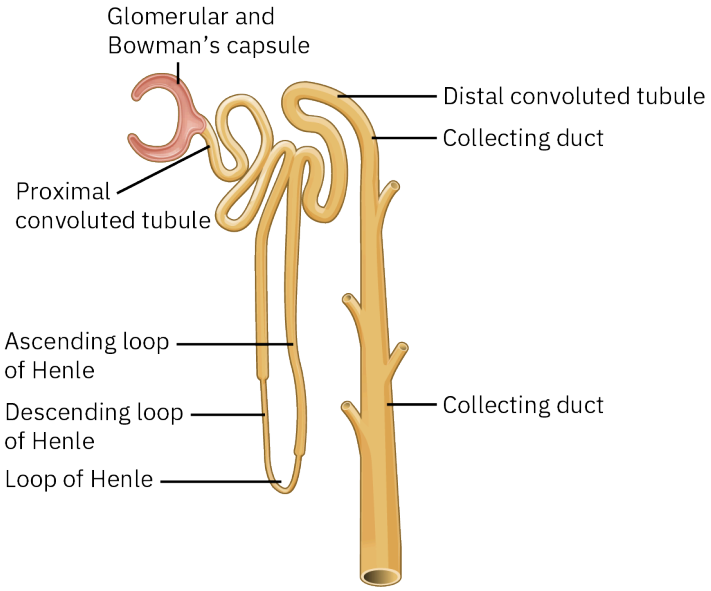


FIGURE 33.3 Various portions of the nephron differ in their capacity to reabsorb water and specific solutes. While much of the reabsorption and secretion occur passively based on concentration gradients, the amount of water that is reabsorbed or lost is tightly regulated. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

There are approximately 1 million nephrons in each kidney. There are two types of nephrons, which are labeled according to their anatomical position. Eighty-five percent of the nephrons are **cortical nephrons**, located in the outer renal cortex and extending partially into the medulla. The nephron loops are short and are supplied by the peritubular capillaries. The **juxtamedullary nephrons** are positioned at the junction of the renal cortex and the renal medulla. The nephron loop extends into the medulla and is surrounded by the vasa recta, a network of capillaries originating from the efferent arteriole. The cortical portion of the juxtamedullary nephron is also surrounded by the peritubular capillaries, which aid in the concentration and volume control of urine.

Blood is filtered by the globe-shaped renal corpuscle, which contains the **glomerulus** and **Bowman's capsule**. The glomerulus is a tufted structure of **fenestrated capillaries** essential to filtration. The glomerulus is enclosed in a double-layered structure, the Bowman's capsule, which has two surfaces, the exterior parietal layer and the interior visceral layer. The parietal layer is composed of squamous epithelial cells. The visceral layer is composed of specialized epithelial cells called podocytes that encircle the glomerular capillaries. Extensions of the podocytes called pedicles also surround the capillaries, forming filtration slits or pores that also aid filtration. The space between the visceral and parietal layers, the capsular space or Bowman's space, becomes the lumen of the renal tubule. The fluid that is filtered from the glomerular capillaries moves to the renal tubule as filtrate.

The **mesangial cells**, located around the glomerular capillaries, regulate the surface area that is available for glomerular filtration. The cells contract in response to the stretch of increased blood in the capillaries, decreasing the surface area. Conversely, the filtration surface area increases when the cells are relaxed. The cells contract in response to angiotensin II and endothelin and relax in response to atrial natriuretic peptides (ANPs) and nitric oxide.

The renal tubule consists of three different areas with specialized structures and functions. Initially, the filtrate flows through the proximal tubule, which has straight sections and "convoluted" sections. This is the longest segment of the renal tubule, and the surface of the lumen has microvilli that increase the filtration surface area.

The second area, the nephron loop (loop of Henle), has two sections: the descending limb and the ascending limb. The descending limb, which consists of simple squamous cells, is often identified as the thin descending limb, whereas the ascending limb is mostly composed of cuboidal epithelial cells and is called the thick ascending limb.

The terminal portion of the nephron, the distal tubule, also contains straight and convoluted sections; however, the structure is composed of simple cuboidal epithelial cells without the microvilli. The fluid leaves the distal tubule and enters the collection system.

The Juxtaglomerular Apparatus

The macula densa cells are located at the boundary between the ascending loop of Henle and the distal tubules. These cells contact the juxtaglomerular cells of the smooth muscles of afferent and efferent arterioles to control **glomerular filtration rate** (GFR) and blood pressure.

Additional Regulatory Functions of the Nephron

Three additional functions of the nephron are important to discuss:

- *Erythropoietin production:* When the partial pressure of dissolved oxygen in the blood (pO_2) is decreased, erythropoietin (EPO), a hormone produced by the peritubular cells in the renal cortex, is released. The EPO stimulates the production of red blood cells by the bone marrow (Schoener & Borger, 2022).
- *Gluconeogenesis:* The proximal tubules of the kidney are responsible for producing 40% of the glucose needed to maintain homeostatic glucose levels. The kidney increases glucose production in response to acidosis or when stimulated by stress hormones such as cortisol (Legouis et al., 2022).
- *Vitamin D_3 conversion:* Vitamin D from the diet and skin absorption is converted to 25-hydroxyvitamin D (25[OH]D) in the liver and then to 1,25-dihydroxyvitamin D, the active form of the vitamin, in the kidneys. Deficient vitamin D levels are associated with altered calcium balance and bone metabolism (Kim et al., 2021).

Glomerular Filtration

Glomerular filtration is the initial step in removing waste and concentrating the urine. The filtration membrane consists of three layers: the fenestrated glomerular capillary endothelial cells, the basal lumina, and the podocytes in the visceral layer of the glomerular or Bowman's capsule. The first layer, the openings in the fenestrated

glomerular capillary endothelial cells, allows the movement of molecules up to 100 nanometers in size, which means that platelets and blood cells are not filtered from the capillaries. The basal lumina is a thin layer of tissue between the glomerular endothelial cells and the podocytes. The collagen fibers from this layer generate a mesh that creates a second barrier. This collagen mesh blocks most plasma proteins by size and also blocks negatively charged proteins regardless of size. The filtration slits or pores formed by the podocytes provide the third barrier to filtration. These openings block plasma proteins from entering the filtrate. The filtrate consists of the fluids and solutes that progress through the filtration membrane. Substances that are commonly included in the filtrate include water, glucose, electrolytes, amino acids, and smaller proteins.

The Glomerular Filtration Rate (GFR)

The kidneys filter approximately 200 liters of fluid every day (Ogobuiro & Tuma, 2022). The normal glomerular filtration rate is 120–125 mL per minute (Ogobuiro & Tuma, 2022). This value is influenced by the client's age, weight, and muscle mass. Filtration is *increased* by the glomerular capillary hydrostatic pressure and Bowman's capsule oncotic pressure, and filtration is *opposed* by the glomerular oncotic pressure and the Bowman's capsule hydrostatic pressure. Note that the oncotic pressure in the Bowman's capsule is normally near zero because proteins and cells do not enter the capsule.

Three elements determine the critical net filtration pressure required for homeostatic glomerular filtration:

- *Glomerular capillary hydrostatic pressure:* The pressure in the glomerular capillary bed is 55 mm Hg and is the major filtration force (Ogobuiro & Tuma, 2022).
- *Glomerular capillary oncotic pressure*: This pressure is determined by the oncotic pressure of the blood in the glomerulus. This pressure is higher than the average oncotic pressure because water is quickly filtered from the blood. This pressure opposes filtration because the increased osmotic pressure can pull the water from the filtrate into the arterioles.
- *Bowman's capsule hydrostatic pressure:* The hydrostatic pressure is determined by the amount of fluid in the capsular space. The amount of fluid is determined by the rate at which the filtrate enters the capsular space, which is greater than the rate at which the filtrate empties into the lumen of the tubule. This pressure opposes filtration.

Autoregulation of the Glomerular Filtration Rate

Autoregulation of the GFR maintains homeostatic renal function when the systemic blood pressure (BP) is abnormally increased or decreased. There are two intrinsic or local renal responses that respond to these alterations: the myogenic response and tubuloglomerular feedback.

Myogenic Response

The myogenic response maintains the renal blood flow at homeostatic levels in response to the stretch of the vascular smooth muscles of the afferent arterioles. When the systemic BP is elevated, the afferent arterioles are stretched and the GFR is increased. The kidney responds by constricting the afferent arterioles, which decreases the blood being filtered, returning the GFR to normal. When the systemic BP is decreased, the afferent arterioles are stretched less than normal and the GFR declines. The kidney responds by dilating the smooth muscles of the arterioles, which increases the renal blood flow and the GFR.

The myogenic response rapidly addresses alterations in the GFR; however, the response only occurs when the systolic blood pressure is 80–180 mm Hg. When the systolic BP is above 180 mm Hg, additional smooth muscle constriction is not possible. Conversely, when the pressure falls below 80 mm Hg, additional dilation of the arterioles will not increase the GFR.

Tubuloglomerular Feedback

The macula densa cells located around the distal tubule react to the changes in the glomerular filtration rate. When the filtration rate increases the amount of sodium and chloride, the ultrafiltrate also increases, which results in additional absorption of these ions by the macula densa cells. The cells respond to these changes by releasing ATP (adenosine triphosphate) from the basolateral membrane, which directly or indirectly constricts the afferent arterioles. The ATP directly constricts the arterioles, and ATP converted to adenosine indirectly constricts the afferent arterioles. This constriction decreases renal blood flow and returns the GFR to normal. When the filtration rate decreases, less sodium and chloride are delivered to the macula densa cells, which triggers dilation of the

afferent arterioles and constriction of the efferent arterioles. This results in increased hydrostatic pressure that returns the GFR to normal. In addition to autoregulation, the tubuloglomerular feedback mechanism also contributes to renal homeostasis by regulating sodium secretion and renin release.

Hormonal Actions Affecting the Glomerular Filtration Rate

Several hormones regulate kidney function by stimulating or inhibiting renal blood flow. Two of these processes are described below.

Renin-Angiotensin-Aldosterone System (RAAS)

The primary function of the RAAS is to control systemic blood pressure and fluid balance; however, the system also contributes to homeostasis of the glomerular filtration rate and tubular reabsorption of electrolytes. Three conditions can trigger the system: sympathetic nerve stimulation, decreased glomerular hydrostatic pressure, and feedback from the macula densa cells in the glomerular feedback system.

In response to decreased renal blood flow caused by decreased systemic blood pressure, the juxtaglomerular cells in the afferent arteriole trigger the release of renin. This action results in the conversion of angiotensinogen from the liver to angiotensin I. In the lung, the angiotensin-converting enzyme converts angiotensin I, activating angiotensin II. Angiotensin II constricts systemic and renal efferent arterioles; prompts reabsorption of sodium, chloride, and water by osmosis from the proximal tubule; releases aldosterone, which further increases sodium ion and water reabsorption in the distal tubule; and stimulates the thirst response.

Atrial Natriuretic Peptides

The atrial natriuretic peptides (ANPs) are released from the atria in response to increased atrial blood volume. The primary purpose of the ANPs is regulation of the systemic blood pressure; however, one part of that process involves increasing the GFR. In the glomerulus, the ANPs dilate the afferent arterioles and constrict the efferent arterioles. This increases the glomerular hydrostatic pressure, resulting in increased GFR, which increases the urinary output and decreases the blood pressure.

Sympathetic Nervous System Effect on the GFR

Stimulation of the sympathetic nervous system regulates blood pressure by constricting systemic blood vessels, including the afferent arterioles. The effect of this stimulation on the GFR varies according to the level of sympathetic response. When the sympathetic stimulation is low due to mild exercise, the juxtaglomerular cells release a weaker form of angiotensin II, which increases the GFR and the systemic BP. Conversely, when sympathetic stimulation is high due to blood loss or strenuous physical activity, large amounts of angiotensin II are secreted, constricting both the afferent and efferent arterioles, which decreases the GFR. This response protects the circulating blood volume.

LINK TO LEARNING

Tubular Reabsorption (https://openstax.org/r/khanacademy)

This article from Khan Academy discusses the process of tubular reabsorption in the nephron.

Tubular Reabsorption

The tubules are responsible for selective reabsorption of electrolytes, nutrients, and water from the filtrate and the return of these substances to the circulating blood volume. These mechanisms are responsible for moving water and substances from one area to another:

- *Active transport:* Active transport uses energy, ATP, to move a substance across a membrane from an area of low concentration to an area of higher concentration of that substance.
- *Diffusion:* Simple diffusion follows the concentration gradient and moves substances across a membrane from an area of higher concentration to an area of lower concentration. This process does not require energy expenditure.
- *Facilitated diffusion:* This process also moves substances along a concentration gradient; however, membrane receptors or channel proteins are required for the transfer (Ogobuiro & Tuma, 2022).
- *Secondary transport systems:* Secondary transport systems, including symport and antiport structures, each

require energy. Symport structures move two or more substances in the same direction simultaneously. Antiport structures move two or more substances across the cell membrane in different directions.

The Proximal Tubule

Approximately 65% of the filtrate is reabsorbed in the proximal tubule. The active transport of elements by the sodium/potassium pumps consumes 6%–8% of the daily ATP expenditure. The microvilli lining the tubule facilitate rapid reabsorption of the following elements to support homeostasis (Zhang & Mahler, 2021):

- Proximal tubular reabsorption
  - *Glucose:* Secondary active transport with sodium
  - *Proteins and amino acids:* Secondary active transport with sodium
  - *Sodium:* Two-thirds actively reabsorbed
  - *Chloride:* Symport reabsorption with sodium, diffusion
  - *Vitamins and lactate:* Reabsorbed
  - *Bicarbonate ions:* Symport reabsorption with sodium
  - *Water:* Two-thirds reabsorbed osmotically
- Loop of Henle reabsorption
  - *Water:* Reabsorbed by osmosis
  - *Sodium:* Reabsorbed by active transport
  - *Chloride:* Reabsorbed by diffusion
- Distal convoluted tubule and collecting duct reabsorption
  - *Water:* Reabsorbed by osmosis
  - *Sodium:* Reabsorbed by active transport
  - *Chloride:* By symport and diffusion
  - *Bicarbonate:* By antiport with chloride
  - *Calcium:* Reabsorbed
  - *Potassium and hydrogen:* Directed by hormones

Concentration of the Urine

The cells in the distal convoluted tubule are responsible for the final concentration of water and solutes in the urine. The remaining water, sodium, chloride, calcium, and bicarbonate ions are reabsorbed as noted above. The cells are hormonally controlled by aldosterone, antidiuretic hormone (ADH), and ANPs. Aldosterone, released by the adrenal cortex, increases cellular permeability to sodium and increases the number of sodium and potassium pumps, which increases sodium reabsorption from the filtrate. ADH is released from the posterior pituitary gland and facilitates water reabsorption by opening the aquaporins in the tubular cells. These cells are impermeable to water when ADH is absent, resulting in large volumes of water in the urine. The ANPs inhibit the action of aldosterone and ADH, resulting in water retention and sodium absorption (Gewin, 2021).

Tubular Secretion

Tubular secretion is the movement of substances from the peritubular vessels into the tubular lumen to be excreted in the urine. The substances either are moved by passive diffusion from the peritubular capillaries into the interstitial space or are transported across the epithelial lumen of the nephron by active transport requiring ATPase. The proximal tubules secrete nitrogenous waste products such as urea, ammonia, and creatinine; excess hydrogen ions; and toxic substances including many protein-bound drugs that do not cross the glomerular basement membrane. The distal tubules secrete potassium and hydrogen ions in response to the hormonal control noted previously.

Common Conditions Affecting Kidney Function

Kidney function is affected by systemic disease, as discussed in the following section; however, several intrinsic/intrarenal conditions can affect renal homeostasis:

- *Congenital abnormalities:* These are alterations in anatomy or physiology that are present at birth. With renal agenesis and renal hypoplasia, the kidneys fail to develop in utero and the infant is born without kidneys (renal agenesis) or with only one kidney (renal hypoplasia). Renal agenesis is incompatible with extrauterine life, and

the infant is often stillborn. The infant can survive with a single kidney; however, additional congenital abnormalities usually threaten the infant's survival.

- *Genetic disorders:* Multiple forms of polycystic kidney disease can present in childhood or adulthood. These fluid-filled cysts interfere with urine formation and increase the risk of infection and hemorrhage. The disease course is complicated by hypertension, progressive loss of kidney function, and pain. Additional renal conditions, such as renal calculi, are also common in this client population.
- *Neoplasms:* General risk factors for renal neoplasms are similar to other types of cancer: smoking, obesity, hypertension, history of renal dialysis or transplant, and exposure to environmental toxins.
  - *Wilms tumor/nephroblastoma:* Presents in childhood with the onset of hypertension and kidney enlargement. It is the most common renal cancer in children and has a 90% five-year survival rate.
- *Acute and chronic pyelonephritis (infection):* The renal system has multiple protective mechanisms against infection; however, the most common infections ascend from the ureters, bladder, and urethra. The usual causative agent is *Escherichia coli.* Infections associated with indwelling urinary catheters are common in hospitalized clients, and these infections can progress to chronic renal failure in susceptible clients.
- *Glomerulopathies:* Glomerulopathies are disorders of the glomerular capillaries. These disorders can be due to systemic, autoimmune, or intrinsic renal alterations. Common manifestations include proteinuria, decreased GFR, hypertension, and edema. These disorders are progressive and commonly result in end-stage renal disease (ESRD).
  - *Nephrotic syndrome:* A disorder associated with massive proteinuria, edema, and hypertension. It commonly progresses to ESRD.
- *Renal calculi:* Also called nephrolithiasis, urolithiasis, or kidney stones; are commonly composed of calcium crystals. Risk factors for stone formation include hypertension, red meat ingestion, obesity, family history of nephrolithiasis, prolonged immobility, vesicoureteral reflux, and hyperparathyroidism. Stones may be asymptomatic and excreted without further intervention; however, large stones can move from the kidney pelvis to the ureteral junction or further in the ureter, causing obstruction and pain (**renal colic**). Lithotripsy or endoscopy may be necessary to remove the obstruction. Preventive measures include maintaining oral fluid intake at 64–96 fluid ounces per day (or approximately 2–3 liters), avoiding additional calcium intake, and limiting dietary sodium and protein (National Kidney Foundation, 2019). Clients with recurrent stone formation require chemical analysis of the stones to address dietary restrictions.

LINK TO LEARNING

Renal Calculi Formation

This brief Medline Plus video (https://openstax.org/r/kidneystones) explains how renal calculi form.

33.2 Renal-Associated Fluid Volume Excess

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 33.2.1 Describe the pathophysiology of fluid volume excess as it relates to the renal system.
- 33.2.2 Identify clinical manifestations related to fluid volume excess as it relates to the renal system.
- 33.2.3 Identify the etiology and diagnostic studies related to fluid volume excess as it relates to the renal system.

Fluid Volume Excess and the Kidneys

Fluid volume excess (FVE) is identified as *hypervolemia*, or increased blood volume. It is related to excessive intake or inadequate output of body water. In critically ill clients, infusion of crystalloid intravenous fluids can cause hypervolemia manifested by FVE. Additional primary causes of FVE include psychogenic water intoxication, syndrome of inappropriate antidiuretic hormone (SIADH), nephrotic syndrome, and liver cirrhosis.

More commonly, FVE is due to damage to the renal system by some other disease state. The compensatory mechanisms that maintain homeostasis can also be diminished or inactivated by inflammatory processes,

infections, vascular compromise, obstruction, nephrotoxic molecules, or genetic defects that affect the kidney. Altered kidney function resulting in FVE is often discussed in terms of prerenal, intrinsic renal (or intrarenal), and postrenal causes.

Prerenal Conditions Associated with Fluid Volume Excess

The most common prerenal causes of FVE are altered renal perfusion due to a significant decrease in the circulating blood volume resulting from hemorrhage, hypovolemia, burns, shock states, myocardial infarction and heart failure, or occlusion or stenosis of the renal artery. The altered oxygen level resulting from decreased perfusion damages the renal tubules, and the resulting FVE is relative to the extent of that damage. Depending on the precipitating cause, the cellular injury may be limited to sloughing of the tubule cells into the lumen of the tubule, or the injury may progress to **tubular necrosis**. Common causes include acute myocardial infarction (AMI), cerebral vascular accident (CVA), and damage from medications or other chemicals.

Intrinsic/Intrarenal Conditions Associated with Fluid Volume Excess

Intrinsic kidney damage resulting in FVE may be due to acute or chronic changes associated with malignant hypertension, ischemia due to transfusion reactions, rhabdomyolysis, nephrotoxic effects of aminoglycoside antibiotics, heavy metals, recreational drugs, contrast media, infections such as acute glomerulonephritis, interstitial diseases including pyelonephritis, acute allergic interstitial nephritis, pressure from tumor growth, or stone formation in the renal pelvis or the ureters. Ischemic damage to the nephrons is intermittently distributed along the nephron, whereas nephrotoxic damage is limited to the proximal tubule.

Postrenal Conditions Associated with Fluid Volume Excess

Obstruction of the urinary tract causes a backflow of urine into the kidneys. This increases intraluminal pressure in the tubules, causes ischemia, and decreases the GFR, resulting in FVE. The common causes of obstruction include benign prostatic hypertrophy, intra-abdominal tumors, neurogenic bladder, and ureteral obstruction that is often caused by edema formation following diagnostic testing.

Clinical Manifestations of Fluid Volume Excess

The manifestations of fluid volume excess may vary according to the specific cause of the excess. Common manifestations of FVE include (Lewis, 2022; Stickel et al., 2019):

- Edema in dependent soft tissues
- Ascites
- Adventitious breath sounds (crackles or rales)
- Jugular vein distention
- Rapid weight gain

Diagnostic Studies

Laboratory tests can indicate how much kidney function has been altered by the underlying cause of the FVE. Fluid volume excess decreases sodium, hematocrit, **blood urea nitrogen (BUN)**, and serum osmolarity values. Common laboratory studies include (American Board of Internal Medicine, 2023; Padilla & Abadie, 2022):

- *Glomerular filtration rate:* The GFR provides the most accurate laboratory assessment of renal function. Measurement of the actual filtration rate is possible; however, the procedures are costly and expose the client to either an insulin infusion or a radioisotope injection. The calculated estimate of the GFR is the result of a mathematical calculation based on the client's serum creatinine level, age, sex, ethnicity and weight. The Modification of Diet in Renal Disease (MDRD) Study equation and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation are the most common equations used for estimating GFR in clients age 18 and over (National Institute of Diabetes and Digestive and Kidney Diseases, n.d.). The value is expressed as the filtration rate in milliliters per minute per average body surface area. The normal range is greater than or equal to 90 mL/minute/1.73 m^2. GFR levels associated with FVE may be initially elevated; however, depending on the cause of the alteration and the resulting tubular damage, the GFR may fall below 60 mL/minute.
- *Sodium:* The normal serum sodium level is 136–145 mEq/L. Hyponatremia results from increased fluid intake and may be manifested by FVE, depending on the client's kidney function. Mildly depressed levels may cause

nausea and malaise. Moderately depressed levels can cause progressive neurological alterations including headache and lethargy progressing to seizures, coma, and death. Pulmonary edema unrelated to cardiac events has also been reported.

- *Blood urea nitrogen (BUN):* The normal BUN ranges from 8–20 mg/dL. The BUN varies inversely with the fluid volume balance; therefore, fluid volume excess will decrease the BUN.
- *Serum albumin:* Decreased serum albumin levels result in the movement of fluid from the vascular space to the interstitial space, which increases edema. The normal range is 3.5–5.5 g/dL.
- *Hematocrit:* The hematocrit value decreases with hypervolemia. The normal range for females is 37%–47%; for males, it is 42%–50%.
- *Serum osmolality:* Serum osmolarity is determined by the concentration of all particles dissolved in a body fluid and is measured as the number of osmoles per liter. The particles are sodium and the sodium anions, which include chloride, bicarbonate, glucose, and urea. Normal serum osmolality is 275–295 mOsm/kg H_2O. Decreased serum osmolarity, or hypo-osmolar serum, can be due to psychogenic polydipsia, SIADH, nephrotic syndrome, or liver cirrhosis (Najem et al., 2022).
- *Urine specific gravity:* The normal specific gravity of urine is 1.005–1.030. The specific gravity of urine is near 1.000 in a state of fluid volume excess, which indicates dilute urine.

Additional diagnostic studies may include:

- Ultrasonography of the abdomen, thorax, and vena cava
- Renal biopsy
- Chest x-ray
- Kidney, ureters, and bladder x-ray
- CT and MRI studies of the kidneys
- Pulmonary artery pressure monitoring
- Central venous pressure monitoring
- Daily weights

Appendix B: Common Abbreviations and Lab Values provides additional reference values.

33.3 Introduction to the Urinary System

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 33.3.1 Describe the structure and function of the urinary system.
- 33.3.2 Discuss common conditions that affect the urinary system.

Urethra

Newly formed urine exits the kidney pelvis, flows through the ureters (see Figure 33.4), and enters the bladder at the trigone on the posterior surface. The volume of urine in the bladder triggers the micturition response, and the urine exits the body through the urethra.

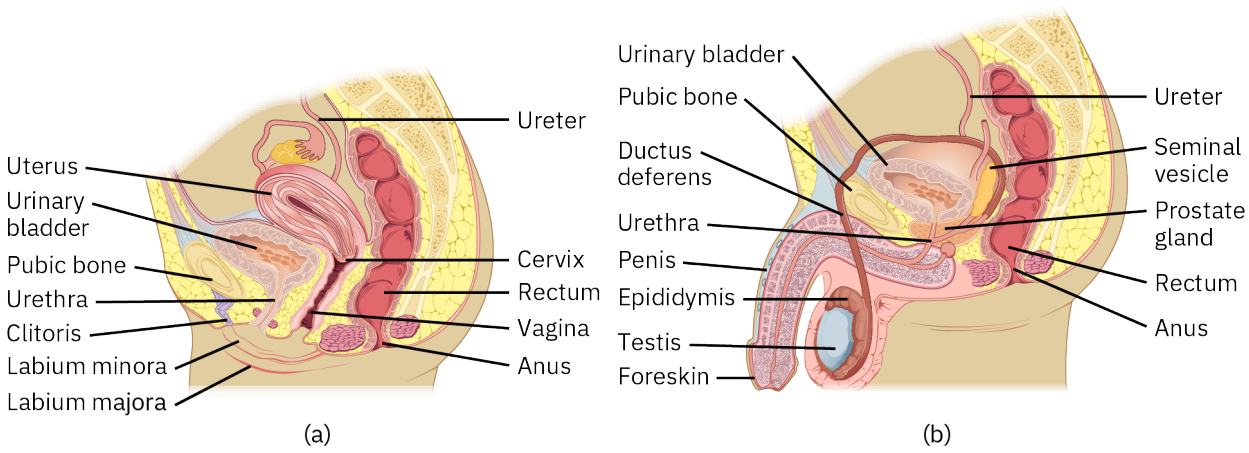


FIGURE 33.4 The urethra transports urine from the bladder to the outside of the body. This diagram shows (a) the female and (b) the male urinary systems. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Bladder

The urinary bladder is a hollow organ suspended from the parietal peritoneum and positioned posterior to the symphysis pubis in the pelvic cavity. The bladder collapses when empty and can expand to accommodate 500–600 mL of urine. The wall of the bladder is composed of three layers. The outer layer, the adventitia, is areolar connective tissue. The middle layer, the detrusor muscle, is composed of multidirectional smooth muscle tissue encircling the urethra at the base of the bladder. The bladder lining is a mucous membrane that is continuous with the urethra. Rugae, or internal folds of the mucosa, are visible when the bladder is empty and accommodate the stretch of the bladder as it fills with urine.

Urine moves from the kidneys through the two ureters, which are approximately 25–30 cm long and 3–4 mm in diameter, and enters the inferior surface of the bladder at the trigone. The ureters tunnel into the bladder surface, and pressure on this area prevents the backflow of urine into the ureter. In addition, internally, sections of bladder mucosal tissue covering the entry of the ureters also inhibit the backflow of urine; this backflow is called **vesicoureteral reflux**.

Micturition Mechanism

Micturition, commonly called *urination*, is the process by which urine is discharged from the bladder. The process is coordinated by the action of the central and peripheral nervous systems on the stretch receptors in the bladder wall, the detrusor muscle fibers, and the internal and external urinary sphincters. Degenerative conditions such as Parkinson disease, multiple sclerosis, and stroke are commonly associated with altered micturition. Spinal cord injuries can disrupt signals to the bladder, causing alterations in the micturition process.

The urge to void is sensed when the bladder contains 150 mL of urine. If this urge is not accommodated, the loss of voluntary control, resulting in urinary incontinence, can occur when the bladder contains 300–400 mL of urine. Once micturition is complete, there is a normal residual volume of up to 50 mL of urine remaining in the bladder (Nandy & Ranganathan, 2022).

Innervation of the Urinary System

The brain and spinal cord must direct the bladder and lower part of the urinary tract to release stored urine. Table 33.1 identifies the three different sets of nerves involved in the micturition process.

Nervous System	Fibers	Function
CNS	PMC	Promotes micturition by coordinating the contraction of the bladder with relaxation of the internal urinary sphincter
	Cerebral cortex	Inhibits micturition by voluntary control of the external sphincter
PNS Autonomic System	Sympathetic fibers	Control vascular supply, mediate the pain receptors, and contribute to relaxation of the bladder
	Parasympathetic sensory fibers	Detect the stretch of the bladder walls as the bladder fills with urine
	Parasympathetic motor fibers	Stimulate contraction of the detrusor muscle
PNS Somatic System	Motor fibers (via the pudendal nerves)	Enable conscious or voluntary control of the external urinary sphincter and micturition

TABLE 33.1 **The Innervation of the Micturition Process** (CNS = central nervous system; PNS = peripheral nervous system; PMC = pontine micturition center)

Common Conditions Affecting the Urinary System

A number of problems can affect the urinary system, including conditions that affect the ability to void properly and infections resulting from bacterial contamination of a normally sterile tract. This section will describe two common conditions, incontinence and urinary tract infection.

Incontinence

As noted in the previous section, micturition is a complex process that requires coordination between the central nervous system and the peripheral nervous system, adequate structure and function of the bladder and urethra, and cognitive control of the process. Urinary incontinence (UI) is defined as the involuntary loss of urine (Tran & Puckett, 2022). The condition is more common in female clients; however, male clients also experience incontinence with associated conditions of the urinary system.

There are multiple forms of UI, including:

- *Urge incontinence:* The client experiences a sudden strong urge to void and frequently does not have sufficient time to respond to the urge before urine leaks from the bladder. It is often the result of an overactive detrusor muscle. Risk factors include age, infection, and obstruction of the bladder outlet by an enlarged prostate gland. This form of UI is also common in clients with degenerative nerve diseases such as Parkinson disease, multiple sclerosis, or a history of stroke, due to CNS damage.
- *Stress incontinence:* This is caused by a sudden increase in intra-abdominal pressure as with sneezing, coughing, and bending, causing the urine to leak from the bladder. This form of UI may be due to loss of pelvic muscle support of the bladder and urethra. Risk factors include estrogen depletion, obesity, childbirth trauma, and cancer therapies. There is also evidence that damage to the spinal nerves due to diabetes may also contribute to the loss of support.
- *Mixed incontinence:* This presents with combined symptoms of urge and stress incontinence. This type of incontinence is prevalent in older female clients.
- *Overflow incontinence:* This type of UI results from obstruction of the urethra, which limits the amount of urine that is emptied with each void. This increases the residual volume of urine, which can lead to stasis of the urine and infection. This condition is most common in older adult male clients with benign prostatic hypertrophy.
- *Functional incontinence:* This form of incontinence results from a factor other than urinary system alterations. It often presents with other deficits such as immobility. The client has an intact urinary system but cannot respond quickly enough to avoid incontinence.

Diagnosis of the type of UI is made through review of the client's voiding diary, review of the client's history, and urodynamic studies. Treatment is aimed at eliminating the underlying cause, strengthening the pelvic floor structures, the use of drugs to modify detrusor activity, and surgery.

CLINICAL TIP

Assessing Incontinence

The voiding diary is one of the most important assessment tools for the diagnosis and treatment of all types of incontinence. The nurse provides the client with basic instructions and a template for recording liquid intake, urinary output, and any occurrences of incontinence. This information can be used by the health care providers to evaluate the client's symptoms.

Urinary Tract Infection

A urinary tract infection (UTI) develops when bacteria enter the urinary system, causing an infection in any part of the urinary tract. As described earlier, pyelonephritis is a kidney infection. Cystitis is bladder inflammation usually caused by bacteria. Risk factors for urinary tract infections include increasing age, female sex, diabetes, obesity, congenital defects, neurogenic bladder, vesicoureteral reflux, and catheterization of the urinary tract. Careful monitoring of susceptible clients is required to prevent recurrent infections. The use of urinary catheters is a significant concern for hospitalized clients. The current recommendation is for short-term use only when necessary. Successful treatment depends on identifying the causative agent and ensuring that all prescribed anti-infectives are consumed.

LINK TO LEARNING

Urinary Stress Incontinence (https://openstax.org/r/picmonic)

This Picmonic online resource reviews the causes and treatments of urinary stress incontinence.

Urethra

The urethra transports urine from the base of the bladder to outside the body. The mucosal lining is composed of transitional epithelium, smooth muscle, and connective tissue. The urine exits the urethra at the external meatus. The internal urinary sphincter, consisting of smooth muscle, surrounds the urethra as it exits the bladder. Control of the internal sphincter is involuntary. The location of the external urinary sphincter is sex-specific and is discussed in the following sections. The two sphincters coordinate the flow of urine from the bladder.

Female Urethra

The female urethra is approximately 3–4 cm long, and the external urinary sphincter surrounds the urethra as it exits the pelvic diaphragm just behind the pubic bone. The urethra is then connected to the anterior vaginal wall, which is a critical requirement for urinary continence. The external urinary meatus is anterior to the vaginal orifice.

Male Urethra

The male urethra is approximately 20 cm in length and carries urine and semen. It consists of four areas. The first section, the preprostatic urethra, which is composed of transitional epithelium tissue, passes from the inferior surface of the bladder to the prostate gland. The second section, the prostatic urethra, is completely encircled by the prostate gland and is approximately 3–4 cm long. The third section, the membranous urethra, goes through the floor of the pelvis and the external urinary urethra and then enters the penis. The final section, the spongy urethra, extends to the tip of the penis, traveling through the corpus spongiosum. This segment of the urethra is approximately 15 cm long.

Chapter Summary

This chapter discussed the renal system, which is responsible for fluid balance, blood pressure regulation, fluid and electrolyte balance, and red blood cell production. It is also responsible for removing metabolic waste products and excess water from the body. The text explained that the nephron is the functional unit of the kidney, and each section of the nephron is responsible for some part of filtration, reabsorption, or secretion. Common conditions affecting these systems were identified. Fluid volume excess, a common manifestation of altered renal system function, was explained as being caused by systemic conditions such as hypertension and heart failure.

Key Terms

blood urea nitrogen (BUN) a blood test that measures the amount of urea nitrogen in the blood; elevated levels can indicate decreased renal function

Bowman's capsule part of the nephron that contains the glomerulus

cortical nephrons comprise a majority of the functional units of the kidney located in the outer renal cortex

fenestrated capillaries small blood vessels in the glomerulus that filter waste

glomerular filtration initial step in making urine involving the filtering of excess fluid and waste products from blood

glomerular filtration rate (GFR) the rate at which the kidneys filter the blood, calculated using the results of blood tests that measure renal function

glomerulus located in nephrons, a tuft of capillaries surrounded by the Bowman's capsule that filters blood

hilum indentation on the medial side of the kidney that allows blood vessels, lymphatic vessels, and nerves to enter and exit

juxtamedullary nephrons nephrons with longer loops of Henle that extend into the medulla

loop of Henle part of the nephron that contributes to absorption of sodium

mesangial cells cells that increase the body surface area for glomerular filtration by limiting the size of molecules that can be filtered

micturition the process through which urine is released from the bladder

nephrons the functional units of the kidney that produce urine

renal colic acute pain associated with kidney stones

renal cortex outermost layer of the internal areas of the kidney containing nephrons

renal medulla inner part of the kidney containing structures essential for regulating urine concentration

renal pelvis funnel-shaped area of the kidney that collects urine and is connected to the ureter

tubular necrosis damage to the tubule cells of the kidney typically resulting from reduced blood flow or chemical exposure

vasa recta long, hairpin-shaped blood vessels that run parallel to the loops of Henle and facilitate water reabsorption

vesicoureteral reflux abnormal backflow of urine from the bladder up through the ureters

Review Questions

1. Which of the following laboratory tests is typically used as an estimate of the glomerular filtration rate?
   a. Hematocrit
   b. BUN
   c. Creatinine
   d. Sodium

2. Which of the following factors favors glomerular filtration?
   a. Hydrostatic pressure in the Bowman's capsule
   b. Oncotic pressure of the glomerular capillaries
   c. Contraction of the mesangial cells
   d. Glomerular capillary hydrostatic pressure

3. Infection is a risk factor for developing which type of incontinence?
   a. Urge
   b. Stress

c. Overflow
d. Functional

4. Which of the following structures contributes to blood pressure regulation?
a. Mesangial cells
b. Vasa recta
c. Epithelial fenestra
d. Juxtaglomerular cells

5. Which of the following effects is consistent with parasympathetic stimulation of the bladder?
a. Urinary reflux
b. Bladder contraction
c. Internal sphincter closure
d. Bladder relaxation

6. The nurse is providing discharge teaching for an adult client who has experienced recurrent renal calculi. Which of these instructions is appropriate for this client?
a. Increase calcium intake.
b. Avoid consuming dark-colored fluids.
c. Increase fluid intake to approximately 2–3 liters each day.
d. Increase protein intake from poultry and fish.

7. The nurse is caring for a client with fluid volume excess. Which of the following manifestations is consistent with this condition?
a. Jugular vein distention
b. Bradycardia
c. Elevated hematocrit
d. Hypotension

8. Which of the following is responsible for forming concentrated urine?
a. Glomerulus
b. Cortical nephron
c. Juxtamedullary nephron
d. Renal pelvis

9. Which of the following conditions is related to overflow incontinence?
a. Estrogen deprivation
b. Urethral obstruction
c. *Escherichia coli* infection
d. Cognitive dysfunction

10. The nurse is caring for a client with renal colic. This finding is most commonly associated with which of the following conditions?
a. Renal calculi
b. Acute tubular necrosis
c. Renal artery stenosis
d. Glomerulonephritis

CHAPTER 34

Diuretic Drugs

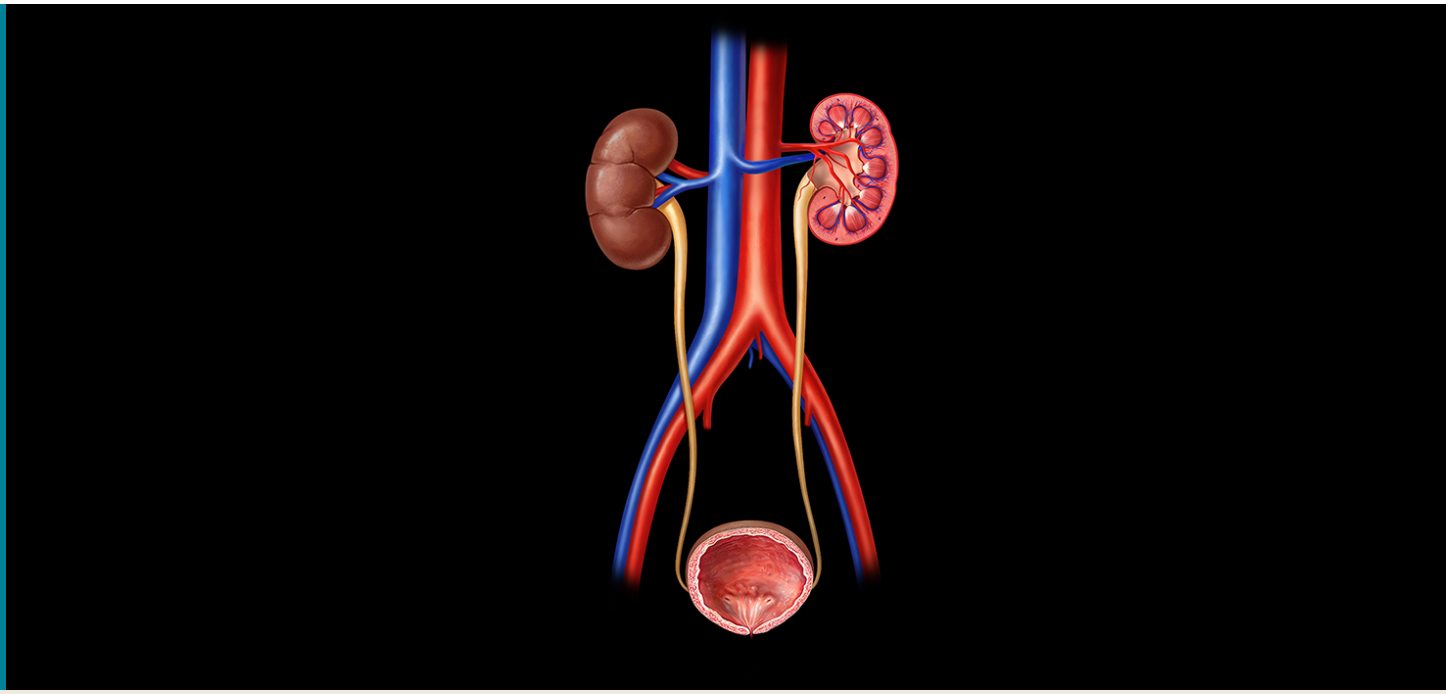


FIGURE 34.1 The renal and urinary system filters out excess fluid and eliminates urea from the body, helping body chemicals stay in balance. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Diuretic therapy is used to increase urinary output for the treatment of edematous conditions, hypertension, heart failure, liver failure, acute and chronic renal diseases, and nephrotic syndrome. There are four groups of diuretics: loop, osmotic, potassium-sparing, and thiazide/thiazide-like. Each targets a specific area of the nephron, resulting in the inhibition of sodium and water reabsorption.

34.1 Introduction to Diuretics

By the end of this section, you should be able to:

- 34.1.1 Discuss fluid volume excess and its impact on renal system disorders.
- 34.1.2 Explain the implications of diuretic use for fluid volume excess with renal system disorders.

Fluid Volume Excess and the Renal System

The renal system normally contributes to the homeostasis of extracellular fluid volume by regulating the **glomerular filtration rate** (GFR), which is the rate at which the kidneys filter blood, and the reabsorption of sodium and water. Successful maintenance of this balance depends on both intrinsic (internal) renal mechanisms and extrinsic (external) systemic mechanisms.

Intrinsic Renal Response to Fluid Volume Excess

Increased fluid volume triggers an intrinsic response from the kidneys, referred to as renal autoregulation.

Autoregulation depends on two physiologic processes: the myogenic response and tubular glomerular feedback. When cardiovascular fluid volume increases, the smooth muscle of the renal blood vessels stretches, stimulating the myogenic response. This response causes afferent arterioles to contract in response to increased volume. In turn, this action decreases the GFR by reducing the blood flow to the renal vessels. The tubuloglomerular feedback process decreases the GFR through the macula densa by reducing sodium reabsorption and inhibiting renin production. These actions by the kidneys are effective only when the pressure in the arterioles is 80–180 mm Hg (Dalal et al., 2022).

Extrinsic Renal Response to Fluid Volume Excess

Outside of the kidneys when there is excess fluid volume, the circulating blood volume increases, stretching the walls of the right atrium and thereby triggering atrial natriuretic peptide (ANP) secretion and reducing secretion of antidiuretic hormone (ADH). The ANP activation dilates afferent arterioles and constricts efferent arterioles, which increases the GFR. The ANP also decreases sodium reabsorption in the collecting duct and inhibits the renin–angiotensin–aldosterone system (RAAS) response to promote vasodilation and sodium excretion. Each nephron segment has a specific sodium entry mechanism that dictates the effect of decreased ADH secretion. In the loop of Henle, the sodium transporting cells respond to decreased ADH levels by reducing the reabsorption of sodium, potassium, and chloride. Decreased ADH secretion also decreases sodium and water reabsorption in the proximal and distal tubules. Under normal circumstances, these actions increase urinary output and decrease fluid volume and blood pressure.

Diuretic Use and the Renal System

Diuretic therapy decreases circulating blood volume to reduce blood pressure and resolve interstitial edema. Diuretic drugs inhibit either the specific sodium reentry mechanism for the nephron segments that regulate sodium, potassium, and chloride or water reabsorption in the proximal and distal tubules. As noted in Figure 34.2, loop diuretics affect sodium, potassium, and chloride levels or reabsorption in the thick ascending loop of Henle. Osmotic diuretics inhibit water reabsorption in the proximal convoluted tubule and the collecting duct. Potassium-sparing diuretics inhibit sodium reabsorption in the collecting tubule, and thiazide and thiazide-like diuretics decrease sodium reabsorption in the distal convoluted tubule. Different diuretics are often used in combination to take advantage of the complementary effects of individual drugs.

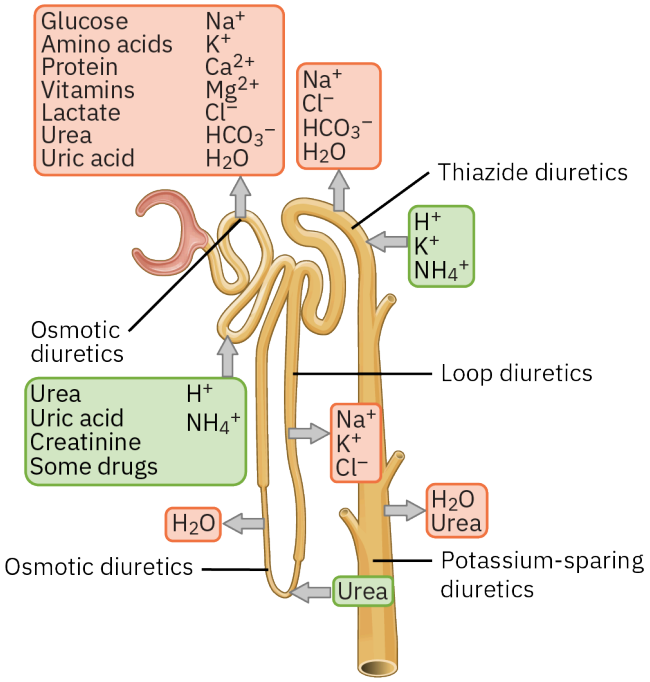


FIGURE 34.2 The active sites of the nephron for the different diuretic types, including loop diuretics, osmotic diuretics, potassium-sparing diuretics, and thiazide and thiazide-like diuretics. (credit: modification of work from *Anatomy and Physiology 2e.* attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Barriers to Effective Treatment

The effectiveness of a specific diuretic is related to its active site in the nephron, its bioavailability, the dosing schedule, and the client's daily salt intake. Under normal circumstances, the kidney quickly reestablishes a balance between sodium intake and sodium and water excretion, so effective diuretic therapy must be appropriately timed. In addition, two compensatory renal responses to diuretic therapy can limit a drug's effectiveness: diuretic resistance and diuretic braking (Wilcox et al., 2020). **Diuretic resistance** occurs when the maximum dose of a loop diuretic fails to produce the anticipated effect on fluid volume status because the successive doses of the drug trigger hypertrophy of the distal tubule, which increases sodium reabsorption. **Diuretic braking** is a progressive decrease in urinary output after repeated doses of loop diuretics. This renal response is due in part to increased sodium reabsorption in the nephron. Chronic diuretic administration also results in decreased fluid volume, which stimulates the RAAS system and increases aldosterone secretion.

Diuretic Therapy for Acute Kidney Injury

Loop diuretics are most frequently prescribed for clients with **acute kidney injury (AKI)** to decrease the risk of additional kidney damage and the development of **hypervolemia**, or fluid overload (Hegde, 2020). Diuretic therapy is not recommended for preventing AKI, and the effectiveness of the therapy is limited in clients with hypoalbuminemia. Hypoalbuminemia commonly occurs in individuals with AKI because loop diuretics are protein bound, meaning they are not filtered by the glomeruli but are delivered directly to the proximal tubules and then secreted into the lumen of the nephrons. Effective diuretic therapy requires administering doses that meet the minimum or threshold dose for the specific drug but do not exceed the ceiling doses, the point at which the drug is no longer effective.

Diuretic Therapy for Chronic Renal Disease

Diuretics are used to treat **chronic renal disease (CRD)**, also referred to as chronic kidney disease (CKD), to regulate fluid volume, increase the effectiveness of other antihypertensive drugs, and lower blood pressure. Standard practice has been to use thiazide and thiazide-like diuretics when the GFR is at or above 30 mL/hour and loop diuretics when the GFR is less than 30 mL/hour (Jo et al., 2023). However, research is being conducted that challenges this practice. Recent research indicates that thiazide and thiazide-like diuretics are safe and effective in clients with chronic renal disease (Teles et al., 2023).

Diuretic Therapy for Nephrotic Syndrome

Nephrotic syndrome is a disorder associated with proteinuria, edema, and hypertension. There is not a consensus regarding the use of diuretic therapy to treat edema secondary to sodium retention and hypoalbuminemia associated with nephrotic syndrome. Loop diuretics are largely protein bound, which means that delivery of the drug to the nephron is less efficient and clearance of the diuretic is increased in those with nephrotic syndrome. Results of research investigating the administration of albumin prior to, or in combination with, loop diuretics to improve delivery of the loop diuretic to the active site in the tubule in clients with hypoalbuminemia are inconclusive. A recent meta-analysis revealed coadministration of albumin with furosemide might enhance diuresis, but further research is needed (Lee et al., 2021). Angiotensin-converting enzyme (ACE) inhibitor drugs or angiotensin II receptor blocker drugs may be used to decrease the renal excretion of albumin, thereby improving the action of the diuretics. Loop diuretics are often used with thiazide or thiazide-like drugs to reduce edema because the combined action may be more effective than either drug type by itself. As noted above, as the GFR declines, the effectiveness of diuretic therapy also declines.

LINK TO LEARNING

Nephron Structure

Access multimedia content (https://openstax.org/books/pharmacology/pages/34-1-introduction-to-diuretics)
The kidney plays an integral role in many body functions. Within the kidney, the nephron is the functional unit carrying out these tasks. Depending on their type, diuretics exert their effects on different parts of the nephron. This Pixorize animation reviews the structure and function of the nephron.

Commonly Assessed Laboratory Tests

Routine blood and urine tests can measure kidney function and indicate kidney damage. A chemistry panel

measures several electrolytes and includes tests that indicate renal function.

Sodium

The therapeutic serum sodium level is 136–145 mEq/L (Padilla & Abadie, 2022). Higher or lower levels can have serious adverse effects. Lower levels, referred to as **hyponatremia**, can cause a range of symptoms. Mild hyponatremia can cause nausea and malaise. Moderate to severe hyponatremia can cause progressive neurologic alterations, including headache and lethargy progressing to seizures, coma, and death. Pulmonary edema unrelated to cardiac events has also been reported. Thiazide diuretic therapy can result in severe hyponatremia, especially in older adults who also consume large amounts of water. **Hypernatremia**, serum sodium levels above the therapeutic range, can cause cognitive dysfunction ranging from lethargy and confusion to seizures. Other signs and symptoms include orthostatic blood pressure changes, tachycardia, oliguria, and dry mucous membranes. Osmotic diuretic administration creates a diuresis that contains water losses in excess of sodium losses.

Potassium

The therapeutic serum potassium level is 3.5–5.0 mEq/L (Padill & Abadie, 2022). Higher or lower levels can have serious negative effects. **Hypokalemia**, or serum potassium levels that are lower than therapeutic, causes muscle weakness. The severity of manifestation depends on the potassium value and the cause and duration of the deficit. Potassium levels around 3.0 mEq/L cause mild to moderate muscle weakness. Potassium levels less than 2.5 mEq/L produce severe muscle weakness, including effects on respiratory muscles and life-threatening electrocardiogram (ECG) changes. Clients taking loop diuretics or thiazide diuretics are at risk for hypokalemia because these medications cause loss of potassium along with sodium. **Hyperkalemia**, or serum potassium levels that are higher than therapeutic, can develop with the use of potassium-sparing diuretics. Mild and moderate hyperkalemia can be asymptomatic, but life-threatening cardiac symptoms or paralysis can occur at levels greater than 6.5 mEq/L. The rate at which the potassium level shifts is more important than the level itself. Clients with chronically elevated potassium levels are less likely to have symptoms, whereas sudden increases are more likely to cause severe symptoms in clients with previously normal potassium levels (Simon et al., 2023).

Blood Urea Nitrogen

The amount of urea nitrogen in the blood, which is one type of waste product in the blood, varies inversely with the estimated GFR (eGFR; see below). However, the blood urea nitrogen (BUN) is also influenced by the client's fluid volume status. The BUN is not identified as a critical indicator of the effectiveness of diuretic therapy. The therapeutic range is 8–20 mg/dL (Padilla & Abadie, 2022).

Creatinine

Serum creatinine is the waste product of muscle tissue metabolism. It is completely cleared by the kidneys, which means that creatinine levels can be used to assess kidney function. Significant renal impairment may occur before the creatinine level increases. The serum creatinine value is used to calculate eGFR. Therapeutic levels vary: 0.5–1.0 mg/dL in females and 0.7–1.2 mg/dL in males (Padilla & Abadie, 2022). Dietary intake of red meat affects creatinine levels.

Serum creatinine and urine creatinine can be compared to estimate renal function; however, the relationship between the two values changes as the GFR falls, and this comparison requires collecting urine over 24 hours as directed. As a result, it is more common to use the serum creatinine level alone. Accurate results from a 24-hour urine collection depend upon the client's ability to follow the protocol for urine collection (Shahbaz & Gupta, 2023).

Glomerular Filtration Rate

The GFR provides the most accurate laboratory assessment of renal function but is not easily measured. The eGFR is calculated based on the client's serum creatinine level, age, sex, and weight. The value is expressed as the filtration rate in milliliters per minute per average body surface area. The therapeutic range in adults is 120–130 mL/minute/1.73 m^2 but can decline with age to about 75 mL/minute/1.73 m^2 at age 70 (Maddukuri, 2022). Levels greater than 180 mL/minute/1.73 m^2 indicate hyperfiltration, which may be the initial sign of diabetes. Decreased filtration rate is associated with advancing age and declining renal function. An eGFR value less than 60 mL/minute/1.73 m^2 for 3 consecutive months indicates chronic renal disease, and an eGFR value less than 15 mL/minute/1.73 m^2 indicates kidney failure or **end-stage renal disease (ESRD)**.

Lipid Profile
Loop diuretics and thiazide and thiazide-like diuretics may increase serum levels of cholesterol, low density lipoprotein (LDL) cholesterol, and triglycerides. All these components are measured in a lipid profile laboratory test.

Uric Acid
Uric acid is a waste product of purine metabolism. It is excreted largely by the kidneys and the gastrointestinal system. Elevated uric acid levels are associated with gout, which is associated with joint and soft tissue injury, most commonly in the big toe. Thiazide and thiazide-like diuretics increase reabsorption of this waste product in the proximal renal tubules. Uric acid is measured in a separate laboratory test. The therapeutic uric acid level is 2.5–8.0 mg/dL (Padilla & Abadie, 2022).

Urinalysis
A urinalysis can detect signs of kidney disease. In addition to measuring creatinine, urine tests determine the presence of uric acid, glucose, and albumin in the urine. Urine osmolality and output are also measured. Therapeutic urine output is 30 mL/hour; an individual is considered oliguric if their urine output is less than 0.5 mL/kg/hour (Berry, 2022).

CLIENT TEACHING GUIDELINES

The client taking a diuretic should:

- Take all diuretics as prescribed by their health care provider.
- Take a baseline pulse and blood pressure measurement before starting the diuretic.
- Monitor and record their pulse and blood pressure regularly to share with their health care provider, reporting any significant changes as defined and directed by the health care provider.
- Maintain adequate intake of fluids as prescribed by their health care provider.
- Follow a low-sodium diet as prescribed by their health care provider.
- Elevate their feet and legs or walk, if they are able, to reduce swelling.
- Take the drug early in the day to avoid **nocturia**.
- Weigh themselves before starting the diuretic and every day at the same time of day. When weighing themselves, clients should use the same scale and wear the same amount of clothing. They should record their weights for review by the health care provider and to be able to track changes.
- Report weight increase of more than 2–3 pounds per day or more than 5 pounds in 1 week.
- Immediately report any concerning symptoms, including difficulty breathing, chest pain, lightheadedness, dizziness with position change, muscle weakness, confusion, significant decrease in urinary output, or irregular heart rate.
- Avoid orthostatic hypotension by changing position slowly and using assistive devices as necessary.

The client taking a diuretic *should not:*

- Change the dose or discontinue the medication without consulting their health care provider.
- Take over-the-counter medications or supplements without consulting their health care provider or pharmacist.

UNFOLDING CASE STUDY

Part A

Read the following clinical scenario to answer the questions that follow. This case study will evolve throughout the chapter.

Gordon Jefferson is a 74-year-old client who presents to his health care provider's office reporting a recent weight gain and lower leg swelling for approximately 1 week.

History

Chronic renal disease
Hypertension

Current Medications
Losartan 50 mg orally daily
Dapagliflozin 10 mg orally daily

Vital Signs		Physical Examination
Temperature:	97.8°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* No jugular vein distention; 2+ peripheral edema noted bilaterally; S1, S2 noted, regular rhythm • *Respiratory:* Respirations unlabored; no adventitious lung sounds • *GI:* Abdomen soft, nontender, nondistended • *GU:* Reports normal urine output • *Neurologic:* Within normal limits • *Integumentary:* No abnormal findings
Blood pressure:	178/92 mm Hg	
Heart rate:	76 beats/min	
Respiratory rate:	20 breaths/min	
Oxygen saturation:	98% on room air	
Height:	5'9"	
Weight:	201 lb	

TABLE 34.1

1. Based on the information above, what diagnosis should the nurse anticipate from the health care provider?
    a. Kidney failure
    b. Arthritis
    c. Edema
    d. Obesity

2. Which diagnostic test would the nurse expect the health care provider to order for Gordon?
    a. Electrocardiogram
    b. Urinalysis
    c. Lipid profile
    d. Chemistry panel

34.2 Loop Diuretics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 34.2.1 Identify the characteristics of loop diuretic drugs used for fluid volume excess and renal system disorders.
- 34.2.2 Explain the indications, actions, adverse reactions, and interactions of loop diuretic drugs used for fluid volume excess and renal system disorders.
- 34.2.3 Describe nursing implications of loop diuretic drugs used for fluid volume excess and renal system disorders.
- 34.2.4 Explain the client education related to loop diuretic drugs used for fluid volume excess and renal system disorders.

Loop diuretics are the most frequently prescribed type of diuretic drug. They are used to treat fluid volume excess and edema associated with heart failure, hypertension, cirrhosis, and renal disease. Loop diuretics act at different points in the nephron to increase sodium and water losses.

Introduction and Use

Loop diuretics increase urinary output by blocking the reabsorption of sodium in the (thick) ascending loop of Henle.

The drugs work by inhibiting the action of the **sodium–potassium–chloride (Na-K-2Cl or NKCC2) cotransporters** in the luminal membrane and increasing water excretion. Blocking the NKCC2 cotransporter blocks potassium reabsorption and triggers calcium and magnesium losses. Loop diuretics are commonly recommended for treating edematous conditions and fluid volume excess associated with heart failure and renal disease. They are approved for treating hypertension but are usually prescribed in combination with other antihypertensives (Huxel et al., 2023). The most frequently used loop diuretics, furosemide, torsemide, and bumetanide, are recommended for treating specific conditions according to their half-life and bioavailability characteristics.

Furosemide, a frequently prescribed loop diuretic, treats edematous conditions and fluid volume excess in heart failure, liver failure, and acute and chronic renal disease, including nephrotic syndrome (Khan et al., 2023). It can be given orally, subcutaneously, intramuscularly, or intravenously. The bioavailability of oral doses of furosemide is approximately 50%, and the drug has a shorter half-life (1.5–2 hours) than other loop diuretics, which means that a continuous intravenous infusion may be more effective than intermittent doses in critically ill clients (Khan et al., 2023). Furoscix was approved in 2022 for subcutaneous delivery of a daily metered dose of furosemide by an on-body infuser for outpatient clients with New York Heart Association class II or III chronic heart failure (Dahiya et al., 2022).This delivery system is intended for clients in the home setting for whom oral furosemide administration has limited effectiveness.

Torsemide exhibits a stronger diuretic effect than furosemide does (Yifan et al., 2021). The drug is used to treat heart failure, hepatic cirrhosis, and chronic renal disease, and it is used with other antihypertensive drugs to treat hypertension (Kanderi & Vaitla, 2023). It can be administered orally or intravenously. The bioavailability of torsemide given by mouth or intravenously is 80%, and the duration of action is 6–8 hours (Kanderi & Vaitla, 2023).

Bumetanide is used to treat clients who do not respond to other loop diuretics, have severe renal disease, or require larger diuretic doses (Sidhu & Puckett, 2023). It is used to manage heart failure, hypertension, hypercalcemia, oliguria, and **ascites** associated with liver failure, and it may also replace furosemide in clients with additional risk factors for **ototoxicity**. The drug can be administered orally, intramuscularly, or intravenously.

Table 34.2 lists common loop diuretics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Furosemide (Lasix, Furoscix)	*Edema due to congestive heart failure, liver cirrhosis, renal disease, or nephrotic syndrome:* 20–80 mg orally daily; maximum daily dose: 600 mg. 20–40 mg intravenously (IV) or intramuscularly, may be repeated in 2 hours. *Hypertension:* 80 mg orally, usually divided into doses of 40 mg twice daily. *Acute pulmonary edema:* 40 mg IV, may be repeated in an hour. *Congestive heart failure:* Subcutaneous administration of Furoscix, 30 mg for the first hour; 12.5 mg/hour for the next 4 hours.
Torsemide (Demadex)	*Congestive heart failure:* Initial dose: 10–20 mg orally or IV once daily. Double the dose as needed until the desired diuretic effect is attained, not to exceed 200 mg. *Chronic renal failure:* Initial dose: 20 mg orally or IV once daily. Double the dose as needed until the desired diuretic effect is attained, not to exceed 200 mg. *Hepatic cirrhosis:* 5–10 mg orally or IV once daily, administered with an aldosterone agonist or potassium-sparing diuretic. Double the dose as needed until the desired diuretic response is attained, not to exceed 40 mg. *Hypertension:* 5 mg orally once daily. If needed after 4–6 weeks, double the dose. If 10 mg is not sufficient, add an additional antihypertensive agent.
Bumetanide (Bumex)	0.5–2 mg orally once daily, initially; may repeat a second or third dose every 4–5 hours as needed until the desired diuretic effect is attained; usual dose: 0.5–2 mg/day; maximum dose: 10 mg/day. 0.5–1 mg IV or intramuscularly once, initially; may repeat a second or third dose every 2–3 hours as needed until the desired diuretic effect is attained; maximum dose: 10 mg/day.

TABLE 34.2 **Drug Emphasis Table: Loop Diuretics** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Loop diuretics primarily cause diuresis-induced electrolyte imbalances (Huxel et al., 2023). These alterations are more common in older adults and clients with inadequate fluid intake. Other common adverse effects include headache, dizziness, and postural hypotension. Metabolic effects may include hyperlipidemia, metabolic alkalosis, and hyperglycemia due to impaired glucose tolerance. Drug-induced pancreatitis also has been reported, most often in clients with a history of pancreatitis. Less common reactions include impotence, thrombocytopenia due to the secretion of antibodies, thrombotic events related to **hypovolemia**, and ototoxicity due to rapid intravenous administration.

Loop diuretics should be used with care in older adults and clients with cardiovascular disease, diabetes, and other risk factors for fluid volume and electrolyte alterations, such as dehydration and increased glucose tolerance. Clients who are allergic to sulfa may possibly experience a mild reaction when using loop diuretics.

Severe dehydration or anuria is a contraindication to any diuretic (Arumugham & Shahin, 2023). Loop diuretics are contraindicated in clients with sensitivity to one of the individual drugs (furosemide, torsemide, or bumetanide) and in clients with Stevens–Johnson syndrome due to the probability of a sensitivity reaction.

Table 34.3 is a drug prototype table for loop diuretics featuring furosemide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Loop diuretic **Mechanism of Action** Inhibits the reabsorption of sodium and water in the ascending loop of Henle, which increases urinary output	**Drug Dosage** *Edema due to congestive heart failure, liver cirrhosis, renal disease, or nephrotic syndrome:* 20–80 mg orally daily; maximum daily dose: 600 mg. 20–40 mg IV or intramuscularly, may be repeated in 2 hours. *Hypertension:* 80 mg orally, usually divided into 40 mg twice daily. *Acute pulmonary edema:* 40 mg IV, may be repeated in an hour. *Congestive heart failure:* Subcutaneous administration of Furoscix, 30 mg for the first hour; 12.5 mg/hour for the next 4 hours.
Indications Hypertension Pulmonary edema Peripheral edema Congestive heart failure **Therapeutic Effects** Lowers blood pressure Decreases edema	**Drug Interactions** ACE inhibitors Metformin Cisapride Diethylpropion Digoxin Dofetilide Ephedrine Lithium Methotrexate Phenytoin Cidofovir **Food Interactions** Foods with high salt content Alcohol Black licorice
Adverse Effects Hypokalemia Hyponatremia Orthostatic hypotension Hypovolemia Hyperglycemia Pancreatitis Azotemia Oliguria Thromboembolism Ototoxicity Agranulocytosis Hyperuricemia	**Contraindications** Anuria Stevens–Johnson syndrome Caution: Renal impairment Older adults Diabetes Hypersensitivity reaction to sulfa or any loop diuretic

TABLE 34.3 **Drug Prototype Table: Furosemide** (source: https://dailymed.nlm.nih.gov/dailymed/)

SPECIAL CONSIDERATIONS

Use of Diuretics in Older Adults

Research indicates that older adults have an increased risk of falling associated with diuretic use. Various adverse effects associated with diuretic use contribute to fall risk, including orthostatic hypotension, increased urine output causing more frequent trips to the bathroom, increased risk of fluid and electrolyte disorders leading to cognitive changes, and effects on bone mass and muscle strength.

(Source: Bai et al., 2023)

SAFETY ALERT

Loop Diuretics

Clients taking both furosemide and digoxin must be monitored for signs of digoxin toxicity, including bradycardia, nausea, vomiting, visual changes (halos), and cardiac arrhythmias. Clients taking loop diuretics as well as lithium must be monitored for toxic blood levels of lithium carbonate, which can develop because diuretics inhibit the kidneys' excretion of the drug.

(Sources: DailyMed, *Furosemide tablet*, 2012; Huxel et al., 2023)

Nursing Implications

The nurse should do the following for clients who are taking loop diuretics:

- Monitor the client for adverse effects related to diuresis.
- Assess the client's blood pressure and heart rate before the initial dose and then intermittently during drug therapy on an ongoing basis to monitor for orthostatic hypotension.
- Assess the client for signs of dehydration, including dry mucous membranes, poor skin turgor, and increased thirst.
- Monitor laboratory results for electrolyte imbalances and signs of renal dysfunction.
- Monitor urine output to evaluate the medication's effectiveness.
- Assess the client's body weight at baseline and on an ongoing basis to monitor fluid retention.
- Assess the client's extremities and dependent areas for edema.
- Assess the client for adverse effects, drug and food interactions, and contraindications.
- Assess the client's understanding of the disease process and the treatment plan, including medication administration, dietary restrictions, and when to call the health care provider.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLINICAL TIP

Intravenous Administration of Furosemide

Furosemide can be administered intravenously as a bolus injection or as a continuous or intermittent infusion for larger doses. A bolus dose should be administered slowly over 1–2 minutes. Rapid infusion rates of loop diuretics may trigger temporary or permanent hearing loss in susceptible clients.

(Source: DailyMed, *Furosemide injection,* 2022)

TRENDING TODAY

Furoscix Subcutaneous Drug Delivery System

A client-administered loop diuretic dosing system was approved in 2022 for the treatment of heart failure. The clinical trial investigators found the client outcomes and pharmacologic features of subcutaneous administration of Furoscix to be equal to those for intravenous administration of furosemide. Watch this brief video demonstration (https://openstax.org/r/furoscix) of its application and use.

(Source: Dahiya et al., 2022)

CLIENT TEACHING GUIDELINES

The client taking a loop diuretic should:

- Follow a modified sodium diet with moderate intake of potassium-rich foods to counteract potassium losses.
- Avoid potential food interactions, including black licorice and alcohol.
- Maintain the prescribed fluid intake to avoid dehydration.
- Monitor for and report any skin changes.
- Change position slowly when going from a lying or sitting position to standing to avoid orthostatic hypotension.
- Notify their health care provider if they experience headaches or dizziness.

The client taking a loop diuretic *should not:*

- Self-adjust a dose without consulting their health care provider.
- Take this medication at night; daytime administration will avoid nocturnal urinary frequency caused by the diuretic effect of the medication.
- Drive or operate machinery if experiencing dizziness.

FDA BLACK BOX WARNING

Loop Diuretics

Loop diuretics can cause severe water loss and electrolyte imbalance when administered at higher dosages.

34.3 Osmotic Diuretics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 34.3.1 Identify the characteristics of osmotic diuretic drugs used for fluid volume excess and renal system disorders.
- 34.3.2 Explain the indications, actions, adverse reactions, and interactions of osmotic diuretic drugs used for fluid volume excess and renal system disorders.
- 34.3.3 Describe nursing implications of osmotic diuretic drugs used for fluid volume excess and renal system disorders.
- 34.3.4 Explain the client education related to osmotic diuretic drugs used for fluid volume excess and renal system disorders.

Osmotic diuretics decrease sodium and water reabsorption in the proximal tubule and the loop of Henle, increasing water loss. Mannitol, the primary osmotic diuretic, is typically used to treat increased intracranial and intraocular pressure.

Introduction and Use

Mannitol is a large sugar molecule that is readily filtered by the glomeruli and is not reabsorbed by the tubules. The resulting osmotic force increases the loss of sodium and water. Although mannitol is also approved to promote diuresis for acute renal failure and for excretion of toxic substances, it is used most commonly to treat increased intracranial pressure and increased intraocular pressure (Tenny et al., 2022). Mannitol reduces intracranial and intraocular pressures by moving water from the cells into the circulation. In the brain, mannitol creates an osmotic gradient that draws water across the blood–brain barrier. In the eye, mannitol draws water from the vitreous humor into the circulation, which decreases the pressure on the retina. Mannitol therapy requires close monitoring because of the risks for fluid volume excess, electrolyte imbalances, and adverse renal and neurologic effects of increased osmotic pressure.

Hypertonic saline solutions may be used in place of mannitol therapy because the saline solution does not cause

hypovolemia in critically ill clients who may already be hypovolemic, hypotensive, or actively bleeding. There is some evidence that hypertonic saline solutions also improve cerebral perfusion and cellular oxygenation (Shi et al., 2020). In addition, in contrast to mannitol, the saline solution can be infused temporarily through a peripheral vein until central venous access is available, and it does not require special reconstitution or delivery systems. Moreover, the therapies are associated with similar clinical outcomes.

Adverse Effects and Contraindications

Mannitol, like other diuretics, can cause electrolyte abnormalities and dehydration. It can cause heart failure secondary to the rapid fluid shift of water into the intravascular space. Administration of the drug has also been associated with the development of AKI in clients with normal renal function. If warm temperatures are not maintained during administration, mannitol can precipitate into crystals, causing vascular and end-organ damage. It is also possible for leakage of mannitol across the blood–brain barrier to cause a rebound increase in intracranial pressure (Tenny et al., 2022).

The client's kidney function must be adequate to manage the increased diuresis that mannitol will produce. It should be avoided in clients with anuria or previous renal damage caused by mannitol, and it should be used with caution in clients with decreased renal function. It should not be used for clients who are severely dehydrated or who have existing electrolyte abnormalities that could be exacerbated by its administration. Mannitol should not be used in clients with congestive heart failure or pulmonary edema.

SAFETY ALERT

Osmotic Diuretics

Renal function should be monitored in all clients receiving mannitol. Acute renal failure can occur not only in clients with preexisting renal disease but also in clients with normal renal function.

(Source: DailyMed, *Mannitol*, 2023)

Table 34.4 is a drug prototype table for osmotic diuretics featuring mannitol. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Osmotic diuretic **Mechanism of Action** Increases osmotic pressure, which increases urinary output	**Drug Dosage** *Increased intracranial pressure:* Bolus injection of 0.25 g/kg IV every 6–8 hours as needed. *Increased intraocular pressure:* 0.25–2 g/kg IV of 20% solution over at least 30 minutes.
Indications Increased intracranial pressure Increased intraocular pressure **Therapeutic Effects** Relieves edema Increases urinary output	**Drug Interactions** Acetaminophen Acetylsalicylic acid (aspirin) Acyclovir Use with caution with all nephrotoxic drugs due to the cumulative effect. **Food Interactions** Alcohol Black licorice
Adverse Effects Hypokalemia Hyponatremia Orthostatic hypotension Hypovolemia Azotemia Oliguria Agranulocytosis Hyperuricemia Heart failure	**Contraindications** Hypersensitivity Anuria Severe hypovolemia Preexisting pulmonary edema Intracranial bleeding Congestive heart failure Impaired renal function Existing electrolyte abnormalities

TABLE 34.4 **Drug Prototype Table: Mannitol** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking mannitol:

- Administer the medication through a dedicated IV line in a large central vein (DailyMed, *Mannitol*, 2023).
- Use only filtered tubing to administer the medication (DailyMed, *Mannitol*, 2023).
- Avoid administering mannitol simultaneously with blood products.
- Check the medication vial for the presence of crystals. If they are present, warm the solution to 140°F, vigorously agitate the vial, and then cool the medication to body temperature before administering (DailyMed, *Mannitol*, 2023).
- Monitor the infusion site for signs of extravasation during administration.
- Carefully monitor the client's fluid volume status by assessing vital signs and weight.
- Monitor lung sounds for congestion and other signs of heart failure or circulatory overload.
- Monitor laboratory values for electrolyte imbalances.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLINICAL TIP

Mannitol Administration

Monitor the insertion site during the infusion for signs of extravasation because extravasation of mannitol can result in the development of compartment syndrome in the arm in which it is infusing. Compartment syndrome is a state of increased pressure in a closed compartment containing bone and fascia, resulting in tissue injury.

(Source: DailyMed, *Mannitol*, 2023)

CLIENT TEACHING GUIDELINES

The client taking an osmotic diuretic should:

- Avoid potential food interactions, including black licorice and alcohol.
- Report any pain, especially headaches or pain at the infusion site.
- Report changes in vision (in clients being treated for increased intraocular pressure).

34.4 Potassium-Sparing Diuretics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 34.4.1 Identify the characteristics of potassium-sparing diuretic drugs used for fluid volume excess and renal system disorders.
- 34.4.2 Explain the indications, actions, adverse reactions, and interactions of potassium-sparing diuretic drugs used for fluid volume excess and renal system disorders.
- 34.4.3 Describe nursing implications of potassium-sparing diuretic drugs used for fluid volume excess and renal system disorders.
- 34.4.4 Explain the client education related to potassium-sparing diuretic drugs used for fluid volume excess and renal system disorders.

Potassium-sparing diuretics increase urinary output by inhibiting sodium reabsorption in the distal tubules and by decreasing potassium and hydrogen ion secretion and blocking the mineral corticoid sites. These drugs are commonly used in combination with other diuretics to modify potassium losses.

Introduction and Use

Potassium-sparing diuretics affect the reabsorption of sodium and the excretion of potassium in the connecting and collecting tubules by inhibiting the sodium transporters and blocking the mineral corticoid receptors. In contrast to the actions of other diuretics, when the potassium-sparing drugs inhibit sodium reabsorption in this area of the nephron, potassium excretion is decreased, thus preserving serum potassium levels.

All potassium-sparing diuretics are used to treat or prevent hypokalemia associated with the use of loop diuretics and thiazide diuretics. The diuretic action of potassium-sparing diuretics is weaker than in other diuretic types, and the onset of action is delayed by as much as 3 days; however, the drugs are often used in combination with more potent diuretics to prevent or treat hypokalemia, heart failure, and hypertension.

Spironolactone is a potassium-sparing diuretic that competes with the aldosterone (mineralocorticoid) receptors in the distal tubule and collecting duct of the nephron. It is approved to treat hypokalemia, primary hyperaldosteronism, heart failure, edema resulting from cirrhosis, and edema resulting from nephrotic syndrome that is resistant to other treatments. Spironolactone is often added as the fourth drug to treat resistant hypertension, which is defined as failure to reach blood pressure target levels when the client is receiving adequate doses of three antihypertensive drugs. In the early landmark Randomized Aldactone Evaluation Study (RALES), spironolactone was found to reduce mortality from all causes by 30% in clients with heart failure (Patibandla et al., 2022). In 2017, the American Heart Association recommended spironolactone as the treatment of choice in clients with class II–IV heart failure with a potassium level less than 5 mEq/L and creatinine clearance greater than 30 mL/hr (Patibandla et al., 2022). In this client population, spironolactone decreased hospital readmission rates, myocardial fibrosis, hypertrophy of cardiac muscle, and extracellular fluid volume. The drug is used off-label as part of gender-affirming hormone therapy and to treat hirsutism (excessive hair growth in a male growth pattern) and acne.

Amiloride is recommended for the treatment of uncomplicated essential hypertension and chronic heart failure (Almajid & Cassagnol, 2022). Several potential off-label uses for amiloride include treatment of increased urinary output associated with lithium therapy, insulin-induced edema, and multiple myeloma. Triamterene is a potassium-sparing diuretic that also increases the excretion of magnesium. Triamterene is used to treat edema associated with heart failure, nephrotic syndrome, ascites due to cirrhosis, hypertension, and hyperkalemia.

Table 34.5 lists common potassium-sparing diuretics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Spironolactone (Aldactone)	*Heart failure:* 25–50 mg orally once daily. *Hypertension:* 25–100 mg orally once daily or in divided doses. *Edema:* 100 mg orally in single or divided doses of 25–200 mg daily. *Hyperaldosteronism:* 100–400 mg daily.
Amiloride (Midamor)	*CHF or hypertension:* 5–20 mg orally daily with food.
Triamterene (Dyrenium)	*Edema associated with congestive heart failure, liver cirrhosis, nephrotic syndrome, secondary hyperaldosteronism, steroid use, or idiopathic causes:* 100 mg orally twice daily titrated to effect up to 300 mg daily.
Eplerenone (Inspra)	*Heart failure post–myocardial infarction:* Initial dose: 25 mg orally once daily, titrated upward to 50 mg once daily; dose may need to be adjusted depending on potassium levels. *Hypertension:* 50 mg orally once daily; can be increased to 50 mg twice daily if needed.

TABLE 34.5 Drug Emphasis Table: Potassium-Sparing Diuretics (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects related to the diuretic action of these drugs include hyperkalemia, hyponatremia, and hyperuricemia, as well as renal tubular necrosis, glucose intolerance, and metabolic acidosis. Endocrine effects of spironolactone therapy include gynecomastia (enlarged breasts), decreased libido, and other feminizing effects in male clients and menstrual alterations in female clients.

Contraindications include anuria, hyperkalemia, and renal insufficiency. These medications should be used with caution in older adults and individuals who have diabetes or gout.

Table 34.6 is a drug prototype table for potassium-sparing diuretics featuring spironolactone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Potassium-sparing diuretics **Mechanism of Action** Opposes the mineralocorticoid receptors that block the action of aldosterone, resulting in decreased reabsorption of sodium and retention of potassium	**Drug Dosage** *Heart failure:* 25–50 mg orally once daily. *Hypertension:* 25–100 mg orally once daily or in divided doses. *Edema:* 100 mg orally in single or divided doses of 25–200 mg daily. *Hyperaldosteronism:* 100–400 mg daily.
Indications Heart failure with reduced ejection fraction Resistant hypertension Primary hyperaldosteronism Edema secondary to cirrhosis or nephrotic syndrome **Therapeutic Effects** Relieves fluid excess Increases urinary output Reduces potassium excretion	**Drug Interactions** Medications that increase serum potassium, including potassium supplements, ACE inhibitors, and angiotensin II receptor blockers (ARBs) Lithium Nonsteroidal anti-inflammatory drugs Digoxin Cholestyramine Acetylsalicylic acid (aspirin) **Food Interactions** Can be taken with or without food but should be taken consistently with respect to food Potassium salt substitutes Potassium-rich food
Adverse Effects Hyperkalemia Hyponatremia Hypotension Bradycardia Hepatic failure Worsening renal function Electrolyte abnormalities such as hyponatremia Gynecomastia	**Contraindications** Anuria Hyperkalemia Severe hypovolemia Addison's disease

TABLE 34.6 **Drug Prototype Table: Spironolactone** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Potassium-Sparing Diuretics

Clients taking potassium-sparing diuretics are accordingly at risk for hyperkalemia and its associated adverse effects. Hyperkalemia can cause arrhythmias and cardiac arrest if untreated.

(Source: Simon et al., 2023)

Nursing Implications

The nurse should do the following for clients taking potassium-sparing diuretics:

- Assess and monitor the client's heart rate and blood pressure and perform a physical assessment to auscultate lung sounds and check for the presence of edema.
- Monitor the client's weight for any significant increases (2 pounds in one day or 5 pounds in 1 week), which could indicate fluid retention.
- Monitor laboratory tests for electrolyte imbalances.
- Monitor the client's ECG for any changes in cardiac rhythm.
- Assess and monitor for drug and food interactions.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional teaching guidelines.

CLINICAL TIP

Dietary Potassium

Clients should be cautioned about consuming salt substitutes, bananas, and other potassium-rich foods when taking potassium-sparing diuretics. Clients often associate "water pills" with the need for additional dietary potassium.

(Source: DailyMed, *Spironolactone,* 2020)

CLIENT TEACHING GUIDELINES

The client taking a potassium-sparing diuretic should:

- Follow a balanced diet with limited intake of potassium-rich foods to decrease the risk of hyperkalemia.
- Take medications consistently regarding food (take either with or without food).
- Report gynecomastia, menstrual irregularities, and the onset of any additional endocrine alterations.

The client taking a potassium-sparing diuretic *should not:*

- Use potassium-based salt substitutes.
- Take nonsteroid anti-inflammatory medications without consulting their health care provider because these can increase potassium levels.

FDA BLACK BOX WARNING

Potassium-Sparing Diuretics

Spironolactone, a potassium-sparing diuretic that also antagonizes aldosterone receptor sites, may cause the development of several tumor types when administered at high doses that exceed current recommendations.

Amiloride, a potassium-sparing diuretic, may cause hyperkalemia, either alone or when combined with hydrochlorothiazide and ACE inhibitors.

Triamterene, a potassium-sparing diuretic, may cause hyperkalemia, either alone or when combined with hydrochlorothiazide. This is more likely to develop in clients with renal impairment and diabetes.

34.5 Thiazide and Thiazide-Like Diuretics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 34.5.1 Identify the characteristics of thiazide and thiazide-like diuretic drugs used for fluid volume excess and renal system disorders.
- 34.5.2 Explain the indications, actions, adverse reactions, and interactions of thiazide and thiazide-like diuretic drugs used for fluid volume excess and renal system disorders.
- 34.5.3 Describe nursing implications of thiazide and thiazide-like diuretic drugs used for fluid volume excess and renal system disorders.
- 34.5.4 Explain the client education related to thiazide and thiazide-like diuretic drugs used for fluid volume excess and renal system disorders.

Introduction and Use

The **thiazide and thiazide-like diuretics** treat hypertension and edema. They are considered first-line therapies for hypertension, although their antihypertensive effects are not well understood. They treat edema related to congestive heart failure, cirrhosis, and acute and chronic renal diseases, including nephrotic syndrome, acute glomerulonephritis, and chronic renal failure. Thiazide and thiazide-like diuretics are frequently used in combination

with other antihypertensives and diuretic types.

Thiazide and thiazide-like diuretics have three major properties: inhibition of sodium reabsorption, increased reabsorption of calcium, and creation of mild extracellular fluid losses:

- Thiazide and thiazide-like diuretics inhibit the reabsorption of sodium in the distal convoluted tubule by competing with chloride on the Na-Cl transporter, resulting in the loss of chloride and the passive loss of sodium; however, the therapy decreases reabsorption of only 3%–5% of the sodium in the filtrate. This transporter is similar to the NKCC in the loop of Henle. The drugs also exert some inhibitory effect on sodium reabsorption in the proximal tubules and the collecting ducts; however, this diuretic action is countered by the additional reabsorption of sodium in the same area of the nephron.
- Thiazide and thiazide-like diuretics increase the rate of calcium reabsorption in two ways. First, the drugs directly increase the reabsorption rate of calcium that normally occurs in the distal tubule. Second, the drugs decrease extracellular fluid volume by limiting reabsorption of sodium, and this volume change indirectly triggers increased calcium reabsorption into the proximal tubule.
- Thiazide and thiazide-like diuretics block sodium reabsorption from the distal convoluted tubule; this can result in hyponatremia, which increases water loss. The drugs also create mild extracellular fluid loss, which can decrease the tubular volume in the loop of Henle, resulting in decreased free water loss.

Hydrochlorothiazide is one of the most commonly used diuretics. Metolazone is a thiazide-like diuretic that, unlike the thiazide drugs, is also effective in chronic renal disease because it does not affect the GFR. In addition, metolazone does not trigger the RAAS, which means that the use of metolazone combined with a loop diuretic can minimize diuretic resistance and increase renal response with fewer adverse effects (Bond et al., 2022). Chlorthalidone is a thiazide-like diuretic with prolonged action (48–72 hours).

Table 34.7 lists common thiazide and thiazide-like diuretics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Hydrochlorothiazide (Hydrodiuril, Microzide)	*Hypertension:* Initial dose: 25 mg orally once daily; may increase dose to 50 mg/day in 1–2 divided doses. *Edema:* 25–100 mg orally daily as a single or divided dose; administration on alternate days or 3–5 days per week may also be effective.
Chlorothiazide (Diuril)	*Edema:* 500–1000 mg IV once or twice daily.
Metolazone (Zaroxolyn)	*Edema:* 5–20 mg orally once daily. *Hypertension:* 2.5–5 mg orally once daily.
Chlorthalidone (Thalitone)	*Hypertension:* 25 mg orally daily; start with lowest dose and titrate to response. *Edema:* 25 mg orally daily; start with lowest dose and titrate to response.

TABLE 34.7 Drug Emphasis Table: Thiazide Diuretics (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

The adverse effects of thiazide diuretics are related to the sodium losses and the ionic imbalance created by those losses (Akbari & Khorasani-Zedah, 2022). Adverse effects include metabolic alkalosis, hypercalcemia, hyperglycemia, hyperuricemia, hyperlipidemia, photosensitivity reactions, hyponatremia due to decreased reabsorption, and hypokalemia due to action of the sodium–potassium pump in the distal convoluted tubule. Their photosensitizing effects also appear to increase the risk of skin cancer (Shin et al., 2019).

Thiazide and thiazide-like diuretics are contraindicated in individuals with sulfonamide allergy. Sensitivity reactions occur most commonly in clients who experience frequent allergic reactions and less commonly than previously believed in sulfa-sensitive clients. Reactions can include rash, hives, angioedema, wheezing, and anaphylaxis (Akbari & Khorasani-Zedah, 2022). Thiazide and thiazide-like diuretics can increase the risk of digoxin toxicity, and the drugs also should not be administered with lithium. Thiazide and thiazide-like diuretics should be used with caution in clients with renal disease and are contraindicated for clients who are anuric.

Table 34.8 is a drug prototype table for thiazide and thiazide-like diuretics featuring hydrochlorothiazide. It lists

drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Thiazide and thiazide-like diuretics **Mechanism of Action** Exact mechanism unknown, but affects electrolyte reabsorption at the distal renal tubule Increases excretion of sodium and chloride	**Drug Dosage** *Hypertension:* Initial dose: 25 mg orally once daily; may increase dose to 50 mg/day in 1–2 divided doses. *Edema:* 25–100 mg orally daily as a single or divided dose; administration on alternate days or 3–5 days per week may also be effective.
Indications Edema related to congestive heart failure, cirrhosis, and acute and chronic renal diseases, including nephrotic syndrome, acute glomerulonephritis, and chronic renal failure Hypertension **Therapeutic Effects** Decreased edema Decreased blood pressure	**Drug Interactions** Lithium Nonsteroidal anti-inflammatory drugs (NSAIDs) Corticosteroids Antidiabetic drugs **Food Interactions** Alcohol
Adverse Effects Electrolyte imbalances Hypotension (including orthostatic hypotension) Renal dysfunction Photosensitivity reactions Erythema multiforme, including Stevens–Johnson syndrome Aplastic anemia	**Contraindications** Sulfa sensitivity Anuria

TABLE 34.8 **Drug Prototype Table: Hydrochlorothiazide** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Thiazide Diuretics

Thiazide diuretics increase the risk for photosensitivity reactions. The client should avoid long periods of sun exposure and should always use sunscreen.

(Source: DailyMed, *Hydrochlorothiazide*, 2018)

UNFOLDING CASE STUDY

Part B

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up to Case Study Part A.

Gordon Jefferson completes his diagnostic evaluation, and the health care provider diagnoses him with edema. He follows up with his health care provider 1 week later to get the results of his diagnostic studies and review his treatment plan. He is prescribed metolazone 10 mg once daily by mouth for his edema.

3. Because of Gordon's history of chronic renal disease, which symptom should the nurse tell him to report immediately if it occurs?
   a. Increased urine output
   b. Decreased urine output

c. Weight loss of 3 pounds in a week
d. Weight gain of 3 pounds in a week

4. Which nonpharmacologic treatment should the nurse question if the health care provider prescribes it for the client?
   a. Eat a low-sodium diet.
   b. Eat a low-potassium diet.
   c. Walk 10 minutes three times a week.
   d. Elevate legs when sitting.

Nursing Implications

The nurse should do the following for clients taking thiazide or thiazide-like diuretics:

- Assess the client's blood pressure before giving the initial dose and then intermittently during drug therapy on an ongoing basis.
- Monitor for evidence of cardiac changes by assessing heart rate and ECG rhythm strips.
- Evaluate the client's response to therapy as evidenced by decreased edema.
- Monitor the client's urine output and laboratory tests for electrolyte imbalances.
- Assess and monitor the client for other adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLINICAL TIP

Accurate Assessment of Client's Fluid Volume Status

Clients with heart failure are often hospitalized to correct fluid volume overload. Nurses are responsible for accurate physical assessment, data collection, and documentation of the client's fluid volume status, which is critical for effective diuretic therapy. The nurse should monitor the client's response to treatment by measuring urine output, monitoring their weight daily, auscultating lung sounds for rales or crackles, and assessing the client's lower extremities and other dependent areas to determine whether the edema is decreasing.

(Source: Malik et al., 2022)

CLIENT TEACHING GUIDELINES

The client taking a thiazide or thiazide-like diuretic should:

- Follow a balanced diet with moderate intake of potassium-rich foods.
- Wear sunscreen and avoid excessive sun exposure because of risk for photosensitivity reactions.

The client taking a thiazide or thiazide-like diuretic *should not:*

- Take nonsteroidal anti-inflammatory drugs.

UNFOLDING CASE STUDY

Part C

Read the following clinical scenario to answer the questions that follow. This case study is a follow-up from Case Study Parts A and B.

Gordon Jefferson is following up with the health care provider 3 months after his initial diagnosis of edema. He reports that the swelling in his legs has improved; however, he is now reporting generalized weakness. The health

care provider examines the client and reviews the chemistry panel results from laboratory work drawn earlier in the morning. Gordon says he has been taking his prescribed medications:

Current Medications
Losartan 50 mg orally daily
Dapagliflozin 10 mg orally daily
Metolazone 10 mg orally daily

Vital Signs		Physical Examination	Chemistry Panel
Temperature:	98.0°F	• *HEENT:* Within normal limits • *Cardiovascular:* No jugular vein distention; S1, S2 noted; trace peripheral edema noted • *Respiratory*: Within normal limits • *GI:* Within normal limits • *GU:* Within normal limits • *Neurologic:* Within normal limits • *Integumentary:* No abnormal findings	*Sodium:* 140 mEq/L *Potassium:* 2.9 mEq/L *BUN*: 24 mg/dL *Creatinine:* 1.4 mg/dL *eGFR:* 40 mL/minute/1.73 m^2
Blood pressure:	138/88 mm Hg		
Heart rate:	76 beats/min		
Respiratory rate:	16 breaths/min		
Oxygen saturation:	98% on room air		
Height:	5'9"		
Weight:	191 lb		

TABLE 34.9

The health care provider diagnoses the client with hypokalemia, prescribes a potassium supplement, and recommends a low-sodium diet with potassium-rich foods.

5. The nurse provides teaching about the new diet to Gordon. Which of the following statements by Gordon indicates a need for further teaching?
   a. "I will limit my intake of green vegetables."
   b. "I am going to start eating a banana a day to keep the doctor away."
   c. "I have a salt substitute I can use on my food to add flavor."
   d. "I am going to cut back on the number of sandwiches I get from the deli."

6. When reviewing Gordon's medications, the nurse should remind him to immediately report which of the following symptoms?
   a. Weight gain of 2 pounds in 1 week
   b. Increased urine output
   c. A slower than normal heart rate
   d. Dry mouth

Chapter Summary

This chapter discussed diuretic drugs, which are used to treat edematous conditions via selective reabsorption of water and sodium in different areas of the nephron, resulting in increased urinary output. The drugs are used individually or in combination with other diuretics to treat congestion associated with heart failure, ascites due to cirrhosis, pulmonary congestion, increased intracranial and intraocular pressure, acute and chronic renal disease, and nephrotic syndrome.

Loop diuretics increase urinary output by blocking the reabsorption of sodium in the (thick) ascending loop of Henle. These drugs work by inhibiting the action of the Na-K-2Cl (NKCC2) cotransporters in the luminal membrane, thereby inhibiting sodium and chloride reabsorption and triggering losses of potassium and magnesium.

Osmotic diuretics work by decreasing sodium and water reabsorption in the proximal tubule and the loop of Henle, which increases water loss. Mannitol, the most commonly used osmotic diuretic, is used to treat increased intracranial pressure and increased intraocular pressure. It is also approved as a diuretic for acute renal failure.

Potassium-sparing diuretics affect the reabsorption of sodium and the excretion of potassium in the connecting and collecting tubules by inhibiting the sodium transporters and blocking the mineral corticoid receptors. When the potassium-sparing drugs inhibit sodium reabsorption in this area of the nephron, potassium excretion is decreased, preserving serum potassium levels.

Thiazide and thiazide-like diuretics have three major properties: inhibition of sodium reabsorption, increased reabsorption of calcium, and creation of mild extracellular fluid losses. The thiazide drugs are considered the first line of treatment for essential hypertension.

Key Terms

acute kidney injury (AKI) a decrease in kidney function that has an abrupt onset and is possibly reversible, manifested by decreased urine output and/or increased serum creatinine; previously known as acute renal failure

ascites abnormal fluid present between the peritoneum and the abdominal organs

chronic renal disease (CRD) a state of progressive decline of kidney function from a glomerular filtration rate of 59 mL/minute/1.73 m^2 to a glomerular filtration rate of less than 15 mL/minute/1.73 m^2

diuretic braking a progressive decrease in urinary output after repeated doses of loop diuretics

diuretic resistance the state in which the maximum dose of a loop diuretic fails to produce the anticipated effect on fluid volume status because successive doses of the drug trigger hypertrophy of the distal tubule, increasing sodium reabsorption

end-stage renal disease (ESRD) the condition that exists when the glomerular filtration rate falls below 15 mL/minute/1.73 m^2

glomerular filtration rate the rate at which the kidneys filter blood; indicates kidney function

hyperkalemia serum potassium level greater than 5.2 mEq/L

hypernatremia serum sodium level greater than 145 mEq/L

hypervolemia body fluid overload, which includes excess fluid volume and edema

hypokalemia serum potassium level less than 3.5 mEq/L

hyponatremia serum sodium level less than 135 mEq/L

hypovolemia decreased extracellular fluid volume associated with sodium and water loss

loop diuretics drugs that interrupt the reabsorption of sodium and water in the loop of Henle, resulting in increased urinary output

nephrotic syndrome a group of renal alterations that result in abnormal renal excretion of large amounts of protein

nocturia the need to frequently void during the night, interrupting sleep

osmotic diuretics drugs that draw fluid from the cells by increasing osmotic pressure

ototoxicity temporary or permanent damage to the inner ear due to drug therapy

potassium-sparing diuretics drugs that interrupt sodium and water reabsorption while retaining potassium and increasing urinary output

sodium–potassium–chloride cotransporter (Na-K-2Cl or NKCC2) a protein that facilitates transport of sodium, potassium, and chloride into cells

thiazide and thiazide-like diuretics drugs that increase urinary output by reabsorbing sodium and retaining potassium in the nephron

Review Questions

1. Which symptom is most likely to occur in a client who is taking furosemide?
   a. Bradycardia
   b. Chest pain
   c. Muscle weakness
   d. More concentrated urine

2. Which statement indicates that the client needs additional education on their newly prescribed medication, amiloride?
   a. "I will take this medication first thing in the morning."
   b. "I will report any weight loss that occurs after I start taking it."
   c. "I will avoid taking nonsteroidal anti-inflammatory medications."
   d. "I will switch to a salt substitute containing potassium chloride."

3. Which eGFR value is consistent with a client who has chronic renal disease?
   a. 90 mL/minute/1.73 m^2
   b. 75 mL/minute/1.73 m^2
   c. 45 mL/minute/1.73 m^2
   d. 120 mL/minute/1.73 m^2

4. Which medication increases solute concentration in the blood to drive fluid shifts for excretion?
   a. Bumetanide
   b. Mannitol
   c. Metolazone
   d. Triamterene

5. The nurse is caring for an older adult female client with a history of osteoporosis who was recently diagnosed with hypertension. Which diuretic would be most appropriate for this client?
   a. Triamterene
   b. Hydrochlorothiazide
   c. Spironolactone
   d. Furosemide

6. Which sign is most concerning for the client receiving mannitol?
   a. Lung congestion and peripheral edema
   b. Increased urine output
   c. Orthostatic hypotension
   d. Elevated blood glucose levels

7. The nurse should monitor the client receiving spironolactone for which adverse effect?
   a. Nausea and vomiting
   b. Increased intracranial pressure
   c. Hearing loss
   d. Cardiac arrhythmias

8. The nurse is providing discharge teaching for a client who was started on a thiazide diuretic during this hospitalization. Which statement indicates that additional instruction is required?
   a. "I'm concerned about getting up to go to the bathroom all night every night."
   b. "I will let the doctor know if I develop leg cramps."
   c. "I need to read food labels to check for salt."
   d. "I need to eat some potassium every day for a month or so."

9. Which medication could be prescribed to treat hyperkalemia?

a. Mannitol
b. Hydrochlorothiazide
c. Spironolactone
d. Furosemide

10. Which of the following statements is correct?
a. Furosemide is an effective treatment for nephrotic syndrome.
b. To be effective, the dose of a diuretic must meet the threshold dose for the drug.
c. Diuretic therapy improves clinical outcomes in clients with acute kidney injury.
d. Oliguria is an absolute contraindication for diuretic therapy.

CHAPTER 35
Urinary and Bladder Disorder Drugs

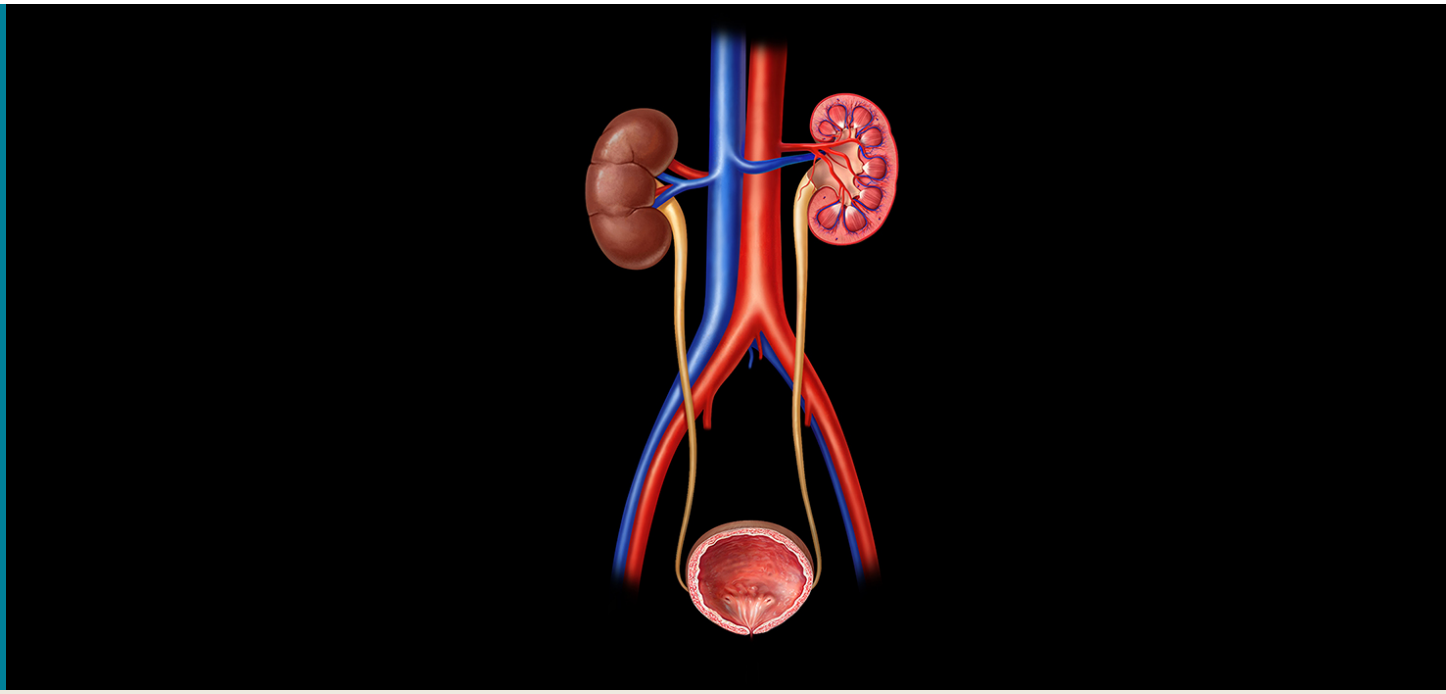


FIGURE 35.1 The renal and urinary system filters out excess fluid and eliminates urea from the body, helping body chemicals stay in balance. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Urinary and bladder disorder drugs are medications used to treat various conditions affecting the urinary system and bladder. These drugs target symptoms or underlying causes of these disorders to alleviate symptoms and improve the function of the urinary system. Commonly used urinary and bladder disorder drugs will be discussed in this chapter.

35.1 Urinary Anti-infectives

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 35.1.1 Identify the characteristics of urinary anti-infective drugs used for urinary and bladder disorders.
- 35.1.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of urinary anti-infective drugs used for urinary and bladder disorders.
- 35.1.3 Describe nursing implications of urinary anti-infective drugs used for urinary and bladder disorders.
- 35.1.4 Explain the client education related to urinary anti-infective drugs used for urinary and bladder disorders.

Urinary **anti-infectives** are a class of drugs specifically used to treat infections of the urinary tract, including the bladder, urethra, ureters, and kidneys (Figure 35.2). They are designed to target and eliminate the bacteria or other

microorganisms causing urinary infection.

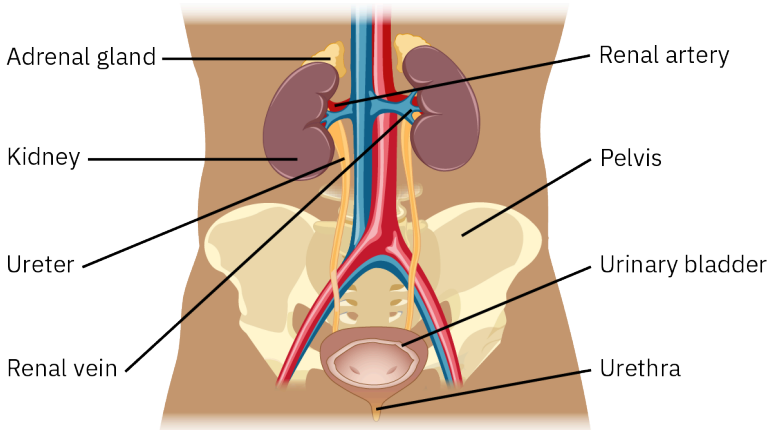


FIGURE 35.2 These structures of the human urinary system are present in both males and females. (credit: modification of work from *Microbiology*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

In this section of the chapter, common urinary anti-infectives will be discussed in greater detail. The choice of medication depends on various factors, such as type of infection, its severity, the presence of underlying conditions, client allergies, and local resistance patterns. The health care provider will prescribe the appropriate urinary anti-infective for the client based on these criteria.

Culture and susceptibility studies should be performed prior to starting urinary anti-infectives. These studies should also be considered when selecting and modifying antibacterial therapy. In the absence of these studies, local epidemiology and susceptibility patterns (e.g., the institutional antibiogram) should be considered for the empiric selection of therapy.

Nitrofurantoin

Nitrofurantoin is specifically indicated for treating urinary tract infections (UTIs) due to susceptible strains of *Escherichia coli*, enterococci, *Staphylococcus aureus*, and certain susceptible strains of *Klebsiella* and *Enterobacter* species (Squadrito & del Portal, 2023).

Adverse reactions can include chronic, subacute, or acute pulmonary hypersensitivity; hepatic reactions, including hepatitis; neurologic conditions such as **asthenia**, vertigo, headache, and drowsiness; **exfoliative dermatitis**; **erythema multiforme**; and gastrointestinal reactions such as nausea, vomiting, abdominal pain, and anorexia. A typical effect of nitrofurantoin is brown discoloration of the urine.

Nitrofurantoin is contraindicated in clients with impaired renal function, impaired hepatic function, or known hypersensitivity. This drug should not be prescribed to pregnant clients after the 37th week of pregnancy, during labor, or when the onset of labor is imminent, because it can lead to a decrease in the fetus's or newborn's red blood cell count. Nitrofurantoin is also contraindicated during lactation and for newborns 1 month old or younger. Nitrofurantoin should be used cautiously in older clients due to potential impaired renal and hepatic function. It is contraindicated in all clients with a creatinine clearance of less than 60 mL due to the increased risk of toxicity because of impaired excretion of the drug. (Nitrofurantoin is in the Beers Criteria® (https://openstax.org/r/agsjournals) list of medications with specific guidelines for use in older clients.)

CLINICAL TIP

Nitrofurantoin and Urine Color

Nitrofurantoin may turn the urine brown. This is an expected effect of the medication and does not harm the client.

Trimethoprim and Sulfamethoxazole

The combination of trimethoprim and sulfamethoxazole (TMP/SMX) is indicated to treat UTIs due to susceptible

strains of *Escherichia coli, Klebsiella* species, *Enterobacter* species, *Morganella morganii, Proteus mirabilis*, and *Proteus vulgaris* (Kemnic & Coleman, 2022). However, it is recommended that initial episodes of uncomplicated UTIs be treated with a single effective antibacterial agent rather than this combination.

The most common adverse reactions are gastrointestinal disturbances, such as nausea, vomiting, and anorexia; **photosensitivity**; and allergic skin reactions such as rash and urticaria. More serious adverse reactions include severe cutaneous reactions, including **Stevens–Johnson syndrome**, as well as **fulminant hepatic necrosis**, **blood dyscrasias**, hyperkalemia, and anaphylaxis or circulatory shock.

TMP/SMX is contraindicated in clients with hypersensitivity to trimethoprim, sulfonamides, or any of their constituents (commonly referred to as "sulfa drugs"); a history of drug-induced immune thrombocytopenia with the use of trimethoprim and/or sulfonamides; megaloblastic anemia due to folate deficiency; or severe renal or hepatic insufficiency. It is also contraindicated in infants younger than 2 months of age and in clients taking dofetilide.

CLINICAL TIP

TMP/SMX and Photosensitivity

TMP/SMX may cause photosensitivity. Nurses should instruct clients to avoid direct sunlight due to the increased risk of sunburn or skin rash with exposure.

Fosfomycin Tromethamine

Fosfomycin tromethamine granules for oral solution are indicated for clients with uncomplicated UTIs (acute cystitis) due to susceptible strains of *Escherichia coli* and *Enterococcus faecalis* (Abbott et al., 2020; DailyMed, *Fosfomycin tromethamine,* 2022).

Adverse effects include diarrhea, vaginitis, nausea, headache, dizziness, asthenia, and dyspepsia. Fosfomycin tromethamine is contraindicated in clients with known sensitivity to the drug or any of its components.

Methenamine Hippurate

Methenamine hippurate tablets are indicated for prophylactic or suppressive treatment of frequently recurring UTIs when long-term therapy is considered necessary. This drug should be used only after other appropriate antimicrobial agents have eradicated the infection (DailyMed, *Methenamine hippurate*, 2021; Heltveit-Olsen et al., 2022).

Minimal adverse effects have been reported with the use of this drug, including nausea, upset stomach, dysuria, and rash. Contraindications include severe renal or hepatic insufficiency and severe dehydration.

Table 35.1 lists common urinary anti-infectives and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Nitrofurantoin (Furadantin, Macrobid, Macrodantin)	100 mg orally twice daily. *Long-term suppressive therapy:* 50–100 mg orally at bedtime. Therapy should be continued for 1 week or at least 3 days after sterility of urine is obtained.
Trimethoprim and sulfamethoxazole (TMP/SMX) (Bactrim, Septra)	*Regular-strength tablet:* one 400 mg/80 mg tablet orally twice daily. *Double-strength tablet:* one 800 mg/160 mg tablet orally twice daily.
Fosfomycin tromethamine (Monurol)	1 sachet (3 g) of granules in 3–4 oz of water for oral solution, taken immediately after combining. Do not use hot water.
Methenamine hippurate (Hiprex)	1 tablet (1 g) orally twice daily (morning and night).

TABLE 35.1 **Drug Emphasis Table: Urinary Anti-infectives** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects of urinary anti-infectives include nausea, vomiting, abdominal pain, anorexia, rash, headache, photosensitivity, and dizziness. Serious adverse effects can occur with certain urinary anti-infectives, including exfoliative dermatitis, Stevens–Johnson syndrome, and fulminant hepatic necrosis.

Contraindications include renal and hepatic insufficiency and hypersensitivity to the drug or any of its components. Certain urinary anti-infectives are contraindicated in clients with blood dyscrasias and in specific pediatric populations.

Table 35.2 is a drug prototype table for urinary anti-infectives featuring TMP/SMX. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anti-infective **Mechanism of Action** Inhibits the bacterial synthesis of tetrahydrofolic acid, which is necessary in the synthesis of thymidine, purines, and bacterial DNA	**Drug Dosage** *Regular-strength tablet:* one 400 mg/80 mg tablet orally twice daily. *Double-strength tablet:* one 800 mg/160 mg tablet orally twice daily.
Indications Treatment of UTIs due to susceptible strains of the following organisms: *Escherichia coli, Klebsiella* species, *Enterobacter* species, *Morganella morganii, Proteus mirabilis*, and *Proteus vulgaris* **Therapeutic Effects** Elimination of bacteria that cause UTIs	**Drug Interactions** Dofetilide Warfarin Nonsteroidal anti-inflammatory drugs Phenytoin Methotrexate Cyclosporine Digoxin Amantadine **Food Interactions** No significant interactions
Adverse Effects Nausea, vomiting, anorexia Rash, urticaria Severe cutaneous reactions Fulminant hepatic necrosis Blood dyscrasias Photosensitivity Hyperkalemia	**Contraindications** Hypersensitivity History of drug-induced immune thrombocytopenia with use of trimethoprim and/or sulfonamides Megaloblastic anemia due to folate deficiency Infants younger than 2 months of age Severe renal or hepatic insufficiency Caution: May cause *Clostridioides difficile*–associated diarrhea

TABLE 35.2 **Drug Prototype Table: Trimethoprim and Sulfamethoxazole (TMP/SMX)** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking urinary anti-infectives:

- Before administering the drug, check the client's medical history, current drug list, and allergies.
- Before administering the drug, confirm the results of baseline laboratory tests, including, but not limited to, urinalysis, urine culture and sensitivity, complete blood cell count, and renal and hepatic function levels.
- For clients receiving nitrofurantoin, monitor for acute and subacute signs of respiratory reactions, such as dyspnea, chest pain, chills, fever, and cough, and notify the health care provider if these develop.
- For clients receiving TMP/SMX, monitor for early signs of blood dyscrasias, such as sore throat, fever, or pallor, and notify the health care provider if these develop.

- Monitor intake, output, and urine specific gravity. Report significant decreases in urinary output to the health care provider.
- Report any signs of superinfection, such as stomatitis, anogenital discharge, or itching, to the health care provider.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a urinary anti-infective should:

- Increase their daily fluid intake (avoiding substances that cause diuresis, such as caffeine), if not contraindicated, to avoid the development of kidney stones.
- Rinse their mouth out thoroughly after taking nitrofurantoin because this drug may stain the teeth.
- Ask the health care provider before taking certain urinary anti-infectives, such as nitrofurantoin, if they are pregnant, are thinking of becoming pregnant, are breastfeeding, or are considering giving these medications to an infant younger than 1 month of age because they may cause serious adverse effects such as blood dyscrasias, anemia, and fetal abnormalities.
- Avoid excessive exposure to sunlight when taking TMP/SMX because photosensitivity may occur, and sun exposure may cause sunburn or skin rash.

The client taking a urinary anti-infective *should not:*

- Crush tablets or open capsules unless directed by a pharmacist because these drugs may cause esophageal or stomach irritation.
- Stop taking the drug unless directed by the health care provider. Drugs in this class help eliminate bacteria in the body and can result in a worsening infection if the drug course is stopped early. Stopping early may also contribute to antibiotic resistance.

FDA BLACK BOX WARNING

Urinary Anti-infectives

Nitrofurantoin may cause acute, subacute, or chronic pulmonary reactions (such as diffuse interstitial pneumonitis or pulmonary fibrosis, or both). Monitoring for these conditions is warranted.

Trimethoprim and sulfamethoxazole (TMP/SMX) may cause acute eosinophilic pneumonia, acute and delayed lung injury, interstitial lung disease, and acute respiratory failure resulting in prolonged mechanical ventilation, extracorporeal membrane oxygenation (ECMO), the need for lung transplantation, or death. Monitoring for these conditions is warranted.

35.2 Urinary Antispasmodics, Antimuscarinics, and Anticholinergics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 35.2.1 Identify the characteristics of urinary antispasmodic, antimuscarinic, and anticholinergic drugs used for urinary and bladder disorders.
- 35.2.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of urinary antispasmodic, antimuscarinic, and anticholinergic drugs used for urinary and bladder disorders.
- 35.2.3 Describe nursing implications of urinary antispasmodic, antimuscarinic, and anticholinergic drugs used for urinary and bladder disorders.
- 35.2.4 Explain the client education related to urinary antispasmodic, antimuscarinic, and anticholinergic drugs used for urinary and bladder disorders.

Urinary **antispasmodics**, **antimuscarinics** (which are a subtype of the cholinergic system), and **anticholinergics** are

different terms used to describe medications that work to relax the detrusor muscles of the bladder and reduce involuntary muscle contractions. These drugs are commonly used to treat conditions characterized by frequent urination, urgency, and sometimes urinary incontinence.

Antispasmodics

Urinary antispasmodics are medications that alleviate spasms or involuntary contractions of the bladder muscles. They affect the urinary detrusor muscle, causing it to relax the bladder, allowing for increased bladder filling and thereby reducing urinary urgency and episodes of urinary incontinence.

Oxybutynin Chloride

Oxybutynin chloride is indicated for the relief of symptoms of bladder instability associated with voiding in clients with detrusor instability due to neurogenic bladder, overactive bladder, or detrusor overactivity (e.g., urgency, frequency, urinary leakage, urge incontinence; Dwyer et al., 2022).

Adverse effects include insomnia, dizziness, headache, blurred vision, dry mouth, constipation, nausea, dyspepsia, **angioedema**, and **urinary retention**. Contraindications include urinary and gastric retention, uncontrolled narrow angle glaucoma, and hypersensitivity to the drug or any of its components.

Mirabegron

Mirabegron is a selective beta-3 adrenoceptor agonist that enhances bladder smooth muscle relaxation and is used to treat overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency (O'Kane et al., 2022).

Adverse effects include hypertension, urinary retention, and angioedema. Contraindications include hypersensitivity to the drug or any of its constituents.

Flavoxate Hydrochloride

Flavoxate hydrochloride counteracts smooth muscle spasm of the urinary tract and exerts its effect directly on the muscle (DailyMed, *Flavoxate hydrochloride*, 2019).

Adverse effects include nausea, vomiting, dry mouth, vertigo, headache, mental confusion, tachycardia, palpitations, urticaria, and blurred vision. It is contraindicated in clients with pyloric or duodenal obstruction, obstructive intestinal lesions or ileus, achalasia, gastrointestinal hemorrhage, or obstructive uropathies of the lower urinary tract.

Antimuscarinics and Anticholinergics

Antimuscarinics are drugs within the anticholinergic class that block the action of acetylcholine, a neurotransmitter involved in muscle contractions, including those of the bladder. (See Drugs to Treat Myasthenia Gravis and Alzheimer's Disease and Drugs to Treat Parkinson's Disease and Multiple Sclerosis for more on muscarinic and cholinergic receptors.) By blocking the effects of acetylcholine, antimuscarinics help reduce the overactivity of the bladder muscles, thereby reducing urgency and urinary frequency (Loloi et al., 2022).

Anticholinergics, like antimuscarinics, block the action of acetylcholine; however, anticholinergics have a broader scope of activity, affecting various organs and systems in the body that are regulated by acetylcholine. In the context of urinary and bladder disorders, anticholinergics work by inhibiting the stimulation of bladder muscles, reducing their contractions and associated symptoms. The term "antimuscarinic" is often used interchangeably with "anticholinergic" when referring to medications used for overactive bladder.

Trospium Chloride

Trospium chloride is indicated for treating overactive bladder with symptoms of urge urinary incontinence, urgency, and urinary frequency (Araklitis et al., 2020).

Adverse effects include dry mouth, constipation, dyspepsia, headache, and urinary retention. Trospium chloride is contraindicated in clients with urinary or gastric retention, uncontrolled narrow angle glaucoma, or hypersensitivity to the drug or any of its components.

Solifenacin Succinate

Solifenacin succinate is used in the treatment of overactive bladder with symptoms of urge urinary incontinence,

urgency, and frequency (Araklitis et al., 2020).

Adverse effects include dry mouth, constipation, UTI, dizziness, blurred vision, dry eyes, and urinary retention. It is contraindicated in clients with urinary and gastric retention, hypersensitivity, or uncontrolled narrow angle glaucoma.

Tolterodine Tartrate

Tolterodine tartrate is indicated for use in clients with an overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency (Narain & Parmar, 2023).

Adverse effects include dry mouth, fatigue, dizziness, constipation, dysuria, dry skin, and weight gain. It is contraindicated in clients with urinary retention, gastric retention, uncontrolled narrow angle glaucoma, or hypersensitivity to the drug or any of its components.

Table 35.3 lists common urinary antispasmodic, antimuscarinic, and anticholinergic drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Oxybutynin chloride (Ditropan, Ditropan XL, Oxytrol)	*Immediate release:* 5 mg orally 2–3 times a day. Maximum dose: 5 mg orally 4 times a day. A lower starting dose of 2.5 mg 2–3 times a day is recommended for frail older adults. *Extended release:* 5–10 mg once daily; adjust dose as needed, depending on response and tolerability, in 5 mg increments every 1–2 weeks (or longer); maximum dose: 30 mg once daily. *Transdermal patch:* 3.9 mg/day applied to dry skin on the abdomen, hip, or buttock twice weekly (every 3–4 days).
Flavoxate hydrochloride (Urispas)	100–200 mg orally 3–4 times a day. With improvement of symptoms, the dose may be reduced.
Mirabegron (Myrbetriq)	Initial dose: 25 mg orally once daily. Depending on individual client efficacy and tolerability, the dose may be increased to 50 mg orally once daily.
Trospium chloride (Trosec)	20 mg orally twice daily at least 1 hour before meals or on an empty stomach. *Clients with severe renal impairment (creatinine clearance less than 30 mL/min):* 20 mg once daily orally at bedtime. *Clients 75 years of age and older:* Dose may be titrated down to 20 mg orally once daily, based on tolerability.
Solifenacin succinate (Vesicare)	5 mg orally once daily. If well tolerated, the dose may be increased to 10 mg orally once daily. *Clients with renal impairment (creatinine clearance less than 30 mL/min):* Do not exceed 5 mg orally once daily.
Tolterodine tartrate (Detrol, Detrol LA)	*Immediate release:* Initial dose: 2 mg orally twice daily. The dose may be lowered to 1 mg orally twice daily based on individual response and tolerability. *Extended release:* 4 mg orally once daily. Swallow whole. *Clients with significantly reduced hepatic or renal function or clients currently taking drugs that are potent inhibitors of CYP3A4:* 1 mg twice daily.

TABLE 35.3 **Drug Emphasis Table: Urinary Antispasmodic, Antimuscarinic, and Anticholinergic Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Typical adverse effects of common urinary antispasmodic, antimuscarinic, and anticholinergic drugs include dry mouth, constipation, nausea, dyspepsia, dizziness, headache, urinary retention, and visual disturbances such as blurred vision and sensitivity to sunlight.

Contraindications include urinary and gastric retention, uncontrolled narrow angle glaucoma, and hypersensitivity to the drug or any of its components.

Table 35.4 is a drug prototype table for the common urinary antispasmodic, antimuscarinic, and anticholinergic drugs featuring oxybutynin chloride. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antispasmodic **Mechanism of Action** Exerts a direct antispasmodic effect on smooth muscle and inhibits the muscarinic action of acetylcholine on smooth muscle, thereby relaxing the detrusor muscle of the bladder and inhibiting the urge to void	**Drug Dosage** *Immediate release:* 5 mg orally 2–3 times a day. Maximum dose: 5 mg orally 4 times a day. A lower starting dose of 2.5 mg 2–3 times a day is recommended for frail older adults. *Extended release:* 5–10 mg once daily; adjust dose as needed, based on response and tolerability, in 5 mg increments every 1–2 weeks (or longer); maximum dose: 30 mg once daily. *Transdermal patch:* 3.9 mg/day applied to dry skin on the abdomen, hip, or buttock twice weekly (every 3–4 days).
Indications Symptoms of bladder instability associated with voiding **Therapeutic Effects** Relief of symptoms of bladder conditions such as urgency, frequency, urinary leakage, urge incontinence, and dysuria	**Drug Interactions** Concomitant use with other anticholinergic drugs Ketoconazole Miconazole Erythromycin Clarithromycin **Food Interactions** No significant interactions
Adverse Effects Insomnia Dizziness Headache Dry mouth Constipation Nausea Angioedema Dyspepsia Urinary retention Visual disturbances such as blurred vision and sensitivity to sunlight	**Contraindications** Hypersensitivity Urinary and gastric retention Uncontrolled narrow angle glaucoma Caution: Central nervous system anticholinergic effects have been reported, including hallucinations, agitation, confusion, and somnolence

TABLE 35.4 **Drug Prototype Table: Oxybutynin Chloride** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking urinary antispasmodics, antimuscarinics, or anticholinergics:

- Before administering the drug, check the client's medical history, current drug list, and allergies.
- Educate the client regarding anticholinergic effects, including dry mouth, urinary retention, constipation, and visual disturbances such as blurred vision and sensitivity to light because these are common adverse effects of these drugs.
- Monitor the client's urine output for signs of urinary retention, such as the inability to empty the bladder, distended bladder, and anxiousness because this is a serious adverse effect, and the client may need an intervention such as a urinary straight catheter to empty the bladder.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a urinary antispasmodic, antimuscarinic, or anticholinergic should:

- Take oxybutynin chloride with water on an empty stomach for better absorption.
- Use sugarless candy, gum, or a saliva substitute for dry mouth, which is an adverse effect of these drugs.
- Wear sunglasses because eye sensitivity, blurred vision, and visual disturbances may occur.
- Increase dietary intake of fiber and increase fluid intake, if not contraindicated, to help reduce the risk of constipation.

The client taking a urinary antispasmodic, antimuscarinic, or anticholinergic *should not:*

- Take additional doses or more oxybutynin chloride than prescribed because doing so can cause serious adverse effects such as urinary retention and urinary infections from reflex.
- Become overheated while taking oxybutynin or urinary antimuscarinics or anticholinergics because these drugs cause body temperature to increase and could lead to heat stroke.
- Take these drugs with alcohol because alcohol may cause increased depression of the central nervous system, resulting in drowsiness, dizziness, and possibly seizures.

FDA BLACK BOX WARNING

Oxybutynin Chloride

Oxybutynin chloride and drugs containing oxybutynin chloride may cause angioedema (swelling similar to hives) of the face, lips, tongue, and/or larynx when taken orally. This condition may interfere with breathing and require hospitalization or emergency treatment. Monitoring is warranted.

35.3 Urinary Analgesics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 35.3.1 Identify the characteristics of urinary analgesic drugs used for urinary and bladder disorders.
- 35.3.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of urinary analgesic drugs used for urinary and bladder disorders.
- 35.3.3 Describe nursing implications of urinary analgesic drugs used for urinary and bladder disorders.
- 35.3.4 Explain the client education related to urinary analgesic drugs used for urinary and bladder disorders.

Urinary analgesics are medications used to relieve pain and discomfort associated with the urinary tract. They are primarily used to treat conditions such as UTIs and **interstitial cystitis** (also known as bladder pain syndrome). Urinary analgesics work by numbing or reducing the sensitivity of the urinary tract, thus alleviating pain during urination.

It is important to note that urinary analgesics do not treat the underlying cause of the pain (such as bacterial infection in the case of UTIs); rather, they provide symptomatic relief. Therefore, it is crucial for the client to consult with a health care provider to determine the cause of urinary pain and to receive appropriate treatment. Additionally, urinary analgesics should be used only as directed and for a limited time because prolonged use without addressing the underlying cause may mask important signs and symptoms and delay appropriate diagnosis and treatment.

Phenazopyridine Hydrochloride

Phenazopyridine hydrochloride, an azo dye, is indicated for the symptomatic relief of pain, burning, urgency, frequency, and other discomfort arising from irritation of the lower urinary tract mucosa caused by infection, trauma, surgery, endoscopic procedures, or the passage of catheters (Eastham & Patel, 2022). This drug should not be used for more than 2 consecutive days to avoid potentially masking a bacterial infection requiring antibiotics.

CLINICAL TIP

Phenazopyridine Hydrochloride and Urine Color

Phenazopyridine hydrochloride may turn the urine, saliva, or tears a reddish-orange color. This is an expected effect of the medication and does not harm the client.

Adverse Effects and Contraindications

Adverse effects include headache; rash; pruritus; gastrointestinal disturbance; reddish-orange color of saliva, tears, or urine; hemolytic anemia; and renal and hepatic toxicity. Phenazopyridine hydrochloride is contraindicated in clients with hypersensitivity and in those with renal insufficiency.

Table 35.5 is a drug prototype table for phenazopyridine hydrochloride. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Urinary analgesic **Mechanism of Action** Exerts an analgesic action locally on the urinary tract mucosa	**Drug Dosage** 200 mg orally 3 times a day after meals. Use should not exceed 2 days.
Indications Symptomatic relief of pain and burning arising from irritation of the lower urinary tract mucosa **Therapeutic Effects** Relief of urinary frequency and urgency and of pain and burning of the urinary tract mucosa	**Drug Interactions** Ketoconazole Lidocaine Procaine Tetracaine **Food Interactions** No significant interactions
Adverse Effects Headache Rash Pruritus Nausea, vomiting Abdominal discomfort Reddish-orange color of saliva, tears, and urine Hemolytic anemia Renal toxicity Hepatic toxicity Yellowish tinge to skin or sclera, which may indicate accumulation due to impaired renal excretion	**Contraindications** Hypersensitivity Renal insufficiency

TABLE 35.5 **Drug Prototype Table: Phenazopyridine Hydrochloride** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking urinary analgesics:

- Before administering the drug, check the client's medical history, current drug list (including over-the-counter medications), and allergies.
- Before administering the drug, assess the client's renal and liver function because these drugs may cause renal or hepatic toxicity in clients who have insufficiency in these areas.
- Notify the health care provider if the client continues to have urinary issues.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a urinary analgesic should:

- Take the medication as directed by their health care provider.
- Report any use of over-the-counter medications that may contain phenazopyridine hydrochloride to the health care provider because concomitant use may cause renal toxicity.
- Report any urinary tract symptoms that do not resolve or worsen to the health care provider because treatment may need to be modified.

The client taking a urinary analgesic *should not:*

- Take extra doses of this medication because doing so may cause serious adverse effects such as hemolytic anemia or renal or hepatic toxicity.
- Wear contact lenses while taking phenazopyridine hydrochloride because it may stain them a reddish-orange.
- Drink alcohol while taking urinary analgesics because their interaction may cause serious effects such as confusion, disorientation, and cardiac arrhythmias.
- Take this medication longer than 2 days because doing so could mask symptoms of a bacterial infection that is not resolving.

35.4 Urinary Stimulants

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 35.4.1 Identify the characteristics of urinary stimulant drugs used for urinary and bladder disorders.
- 35.4.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of urinary stimulant drugs used for urinary and bladder disorders.
- 35.4.3 Describe nursing implications of urinary stimulant drugs used for urinary and bladder disorders.
- 35.4.4 Explain the client education related to urinary stimulant drugs used for urinary and bladder disorders.

Urinary stimulants stimulate the smooth muscles of the urinary bladder. These drugs work by activating the muscarinic receptors of the bladder, leading to increased bladder contractions and improved bladder emptying. They are primarily prescribed for urinary retention or to improve bladder function in individuals with certain neurologic conditions, such as a spinal cord injury.

Bethanechol Chloride

Bethanechol chloride (Duvoid) is indicated for acute postoperative and postpartum nonobstructive (functional) urinary retention and for neurogenic atony of the urinary bladder with retention (Padda & Derain, 2022).

Determine the minimum effective dose by giving 5–10 mg initially and repeating the same amount at hourly intervals until a satisfactory response occurs or until a maximum of 50 mg has been given (DailyMed, *Bethanechol chloride*, 2022).

The drug's effects sometimes appear within 30 minutes, usually peak between 60 and 90 minutes, and persist for approximately 1 hour (DailyMed, *Bethanechol chloride*, 2022).

Adverse Effects and Contraindications

Common adverse effects include malaise, urinary urgency, headache, **vasomotor response**, sweating, and miosis. Contraindications include hyperthyroidism, peptic ulcer disease, asthma, pronounced bradycardia, hypotension, coronary artery disease, seizure, Parkinson's disease, and hypersensitivity to the drug or any of its components.

Table 35.6 is a drug prototype table for urinary stimulants featuring bethanechol chloride. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Urinary stimulant, cholinergic **Mechanism of Action** Stimulates activation of the parasympathetic nervous system, causing increased tone of the detrusor muscle of the bladder, producing contraction and emptying of the bladder	**Drug Dosage** 10–50 mg orally 3–4 times a day.
Indications Treatment of acute postoperative and postpartum nonobstructive (functional) urinary retention Neurogenic atony of the urinary bladder with retention **Therapeutic Effects** Minimizes urinary retention	**Drug Interactions** Atropine Diphenhydramine Donepezil Glutamine Hyoscyamine Neostigmine Procainamide Propantheline Scopolamine **Food Interactions** No significant interactions
Adverse Effects Malaise Headache Urinary urgency Sweating Vasomotor response Miosis Monitor closely for bacteremia due to reflex infection from incomplete bladder emptying	**Contraindications** Hypersensitivity Hyperthyroidism Peptic ulcer disease Asthma Bradycardia Hypotension Coronary artery disease Seizures Parkinson's disease

TABLE 35.6 **Drug Prototype Table: Bethanechol Chloride** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking urinary stimulants:

- Before administering the drug, check the client's medical history, current drug list (including over-the-counter medications), and allergies.
- Monitor the client closely for vasomotor responses, such as hypotension, bradycardia, and orthostatic hypotension.
- For a client taking bethanechol chloride, monitor closely for bronchospasm, wheezing, and tachycardia because these can be serious adverse effects of the drug.
- Monitor the client's urine output closely.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a urinary stimulant should:

- Take the medication as prescribed by their health care provider.
- Take bethanechol chloride on an empty stomach, at least 1 hour before or 2 hours after a meal, for better absorption.

- Notify their health care provider if symptoms do not improve within 90 minutes after taking bethanechol chloride because the treatment may need to be modified.
- Store bethanechol chloride at room temperature and away from moisture and heat.
- Avoid getting up too fast from a sitting or lying position because this drug may cause a vasomotor response that includes dizziness.

The client taking a urinary stimulant *should not:*

- Take two or more doses at one time because this may cause a significant vasomotor response such as severe hypotension and bradycardia.

35.5 Phosphodiesterase 5 Inhibitors

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 35.5.1 Identify the characteristics of phosphodiesterase 5 inhibitors used to treat benign prostatic hyperplasia.
- 35.5.2 Explain the indications, actions, adverse reactions, contraindications, and interactions of phosphodiesterase 5 inhibitors used to treat benign prostatic hyperplasia.
- 35.5.3 Describe nursing implications of phosphodiesterase 5 inhibitors used to treat benign prostatic hyperplasia.
- 35.5.4 Explain the client education related to phosphodiesterase 5 inhibitors used to treat benign prostatic hyperplasia.

Phosphodiesterase 5 (PDE5) inhibitors are a class of medications primarily used to treat erectile dysfunction and, in some cases, pulmonary hypertension and **benign prostatic hyperplasia (BPH)**. These drugs work by blocking the action of an enzyme called phosphodiesterase type 5, which is responsible for breaking down cyclic guanosine monophosphate (cGMP) in the body; cGMP is a molecule that plays a crucial role in relaxing smooth muscles and increasing blood flow to various tissues, including the penis and the lungs.

Tadalafil

Tadalafil (Cialis) is the PDE5 inhibitor that has been approved by regulatory agencies to treat both erectile dysfunction and lower urinary tract symptoms associated with BPH. This chapter covers tadalafil in relation to BPH only. Tadalafil works by relaxing the smooth muscles in the prostate and bladder, which can help improve urine flow and reduce the urinary symptoms caused by prostate enlargement. These effects are achieved through the drug's effect on cGMP, the same pathway that plays a role in erectile function.

Adverse Effects and Contraindications

Common adverse effects include headache, dyspepsia, back pain, myalgia, nasal congestion, pain in limbs, flushing, cough, and UTI. The drug is contraindicated in clients who are taking nitrates or guanylate cyclase stimulants or who are hypersensitive to the drug or any of its components (DailyMed, *Tadalafil,* 2023).

Table 35.7 is a drug prototype table for phosphodiesterase 5 inhibitors for treatment of BPH featuring tadalafil. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Phosphodiesterase 5 inhibitor **Mechanism of Action** Increases cGMP levels Promotes the relaxation of smooth muscles in the prostate and the bladder neck	**Drug Dosage** *For BPH:* 5 mg orally once daily, taken at approximately the same time every day. *For renal impairment, creatinine clearance 30–50 mL/min:* Initial dose: 2.5 mg orally; an increase to 5 mg may be considered based on individual response. *Creatinine clearance less than 30 mL/min or clients receiving hemodialysis:* Tadalafil tablets for once-daily use are not recommended.
Indications Treatment of erectile dysfunction Treatment of the signs and symptoms of benign prostatic hyperplasia **Therapeutic Effects** Alleviates urinary symptoms related to benign prostatic hyperplasia	**Drug Interactions** Nitrates Alpha blockers CYP3A4 inhibitors Antihypertensives Guanylate cyclase stimulants Substantial consumption of alcohol **Food Interactions** No significant interactions
Adverse Effects Headache Dyspepsia Back pain Myalgia Nasal congestion Pain in limbs Flushing Cough UTI Sudden vision or hearing loss Prolonged erection or priapism	**Contraindications** Nitrates Guanylate cyclase stimulants Hypersensitivity reactions

TABLE 35.7 **Drug Prototype Table: Tadalafil** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking PDE5 inhibitors to treat BPH:

- Before administering the drug, check the client's medical history, current drug list (including over-the-counter medications and alcohol), and allergies.
- Before administering the drug, determine the client's regular or intermittent use of organic nitrates. Concomitant use of these with tadalafil can cause a sudden drop in blood pressure to an unsafe level, resulting in dizziness, syncope, or myocardial infarction (DailyMed, *Tadalafil tablet*, 2023).
- Monitor for erections lasting longer than 4 hours and for priapism (painful erections lasting longer than 6 hours).
- Monitor closely for sudden vision or hearing loss because this can be a serious adverse effect of tadalafil.
- Provide client teaching regarding the drug and when to call the health care provider. See below for additional client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a PDE5 inhibitor for BPH should:

- Take the medication as prescribed by their health care provider.
- Notify their health care provider if sudden symptoms of vision or hearing loss occur or if they have an

erection lasting longer than 4 hours or a painful erection lasting longer than 6 hours.
- Avoid getting up too fast from a sitting or lying position because this drug may cause a vasomotor response that includes dizziness.

The client taking a PDE5 inhibitor for BPH *should not:*

- Take tadalafil with nitrates, antihypertensives, alpha blockers, or CYP3A4 inhibitors because concomitant use may cause serious adverse effects, such as an unsafe drop in blood pressure, dizziness, and syncope.
- Consume substantial amounts of alcohol with tadalafil due to hypotensive effects.

Chapter Summary

Urinary and bladder disorder drugs play a crucial role in the treatment of various conditions that affect the urinary system and bladder. These medications are designed to address specific symptoms or underlying conditions of these disorders, aiming to alleviate the individual's discomfort and enhance the overall function of their urinary system.

In this chapter, a comprehensive analysis of commonly used urinary and bladder disorder drugs was presented. The chapter delved into the various classes of medications, such as urinary anti-infectives; antispasmodic, antimuscarinic, and anticholinergic drugs; urinary analgesics; urinary stimulants; and phosphodiesterase 5 inhibitors.

The chapter also highlighted the importance of a tailored treatment approach, considering individual client factors and the specific characteristics of each condition. Safety considerations, potential adverse effects, and efficacy profiles of these medications were also addressed, providing a comprehensive explanation of their therapeutic potential to improve urinary function and alleviate symptoms.

By understanding the different classes of drugs available and the particular aspects of urinary and bladder disorders, such as infections, muscle spasms, and abnormal contractions, nurses can tailor care plans to meet the specific needs of clients with urinary and bladder disorders.

Key Terms

angioedema a reaction similar to hives that results in swelling of the face, lips, tongue, and/or larynx
anti-infectives a class of drugs that work to prevent or treat infections
anticholinergics a class of drugs that block the action of acetylcholine, thereby inhibiting nerve impulses responsible for involuntary muscle movements
antimuscarinics a class of drugs that decrease smooth muscle motility in the urinary tract, increasing the tone of the urinary sphincter and controlling urination
antispasmodics a class of drugs that are used to control spasms of the stomach, intestines, and bladder
asthenia weakness; lack of energy or strength
benign prostatic hyperplasia (BPH) enlargement of the prostate gland
blood dyscrasias a nonspecific term used to describe any blood-related diseases or conditions
erythema multiforme a skin disorder characterized by bulls-eye–shaped lesions (a pink center surrounded by a pale border and outer pink ring) that are painful and itchy
exfoliative dermatitis a skin condition that causes shedding of the top layer of skin
fulminant hepatic necrosis severe, acute liver failure
interstitial cystitis a disorder that causes the bladder to store urine before it is passed out of the body, resulting in bladder pain and pressure
phosphodiesterase 5 (PDE5) inhibitors a class of drugs primarily used to treat erectile dysfunction and, in some cases, pulmonary hypertension and benign prostatic hyperplasia
photosensitivity an increased sensitivity to sunlight or artificial light
Stevens–Johnson syndrome a rare and serious condition of the skin and mucous membranes that causes a painful rash and blisters; can be life-threatening
urinary analgesics a class of drugs used to relieve pain and discomfort associated with the urinary tract
urinary retention a condition in which the bladder does not completely empty; the sudden inability to urinate
urinary stimulants a class of drugs that stimulate the smooth muscles of the urinary bladder
vasomotor response systemic vasodilation resulting in vertigo and syncope with changes in body position

Review Questions

1. A client is receiving trimethoprim and sulfamethoxazole for a urinary tract infection. The nurse should monitor the client for which potential adverse effect?
   a. Photosensitivity
   b. Hypoglycemia
   c. Tinnitus
   d. Hypertension

2. The health care provider prescribes phenazopyridine hydrochloride 200 mg orally three times daily for a

client with urinary tract discomfort. The available tablets are 100 mg each. How many tablets should the nurse administer per dose?

a. 1 tablet
b. 2 tablets
c. 3 tablets
d. 4 tablets

3. A 65-year-old male client presents to the urology clinic with lower urinary tract symptoms including frequency and hesitancy. After a thorough assessment, the client is diagnosed with benign prostatic hyperplasia (BPH) and is prescribed tadalafil. The client is concerned about the effectiveness of tadalafil for BPH. What information should the nurse include in their response to address the client's concerns?

a. Tadalafil primarily treats BPH by reducing prostate size.
b. Tadalafil is not effective for treating BPH and is primarily used for erectile dysfunction.
c. Tadalafil can help improve BPH symptoms by relaxing the muscles in the prostate and bladder neck.
d. Tadalafil is the first-line treatment for BPH and is recommended for all clients with this condition.

4. A nurse is caring for a client with an overactive bladder who is prescribed oxybutynin. Which adverse effect will the nurse include when educating the client about this medication?

a. Diarrhea
b. Urinary urgency
c. Dry mouth
d. Restlessness

5. A nurse is caring for a client with urinary tract discomfort. The health care provider prescribes phenazopyridine hydrochloride. The nurse instructs the client that this drug is classified as an:

a. Antispasmodic drug
b. Analgesic drug
c. Anti-infective drug
d. Anticholinergic drug

6. The nurse is providing discharge teaching for a client who has a new prescription for tadalafil. The nurse will caution the client about which of the following side effects?

a. Angioedema
b. Urinary urgency
c. Hemolytic anemia
d. Vasomotor response

7. Which statement accurately describes the pharmacologic action of mirabegron?

a. Stimulates the alpha-adrenergic receptors
b. Inhibits acetylcholinesterase activity
c. Relaxes smooth muscle in the bladder
d. Blocks angiotensin II receptors

8. Which of the following is the potential effect of trimethoprim and sulfamethoxazole on potassium levels in a client?

a. Hyperkalemia
b. Hypokalemia
c. No effect on potassium levels
d. Variable effect on potassium levels

9. A nurse is providing discharge instructions to a client who has been prescribed, concomitantly with fosfomycin, phenazopyridine hydrochloride for symptomatic relief of urinary pain and discomfort. Which statement by the client indicates a need for further education regarding the use of phenazopyridine

hydrochloride?

a. "I should expect my urine to turn orange or reddish in color."
b. "I will take this medication with meals to minimize stomach upset."
c. "I understand that this medication may stain my contact lenses."
d. "I will continue taking this medication until my symptoms completely resolve."

10. A client with a history of narrow angle glaucoma has been prescribed solifenacin succinate for overactive bladder. The nurse should take which action regarding the medication?

a. Administer the medication as prescribed and monitor the client's intraocular pressure closely
b. Administer a reduced dosage of the medication to prevent glaucoma exacerbation
c. Do not administer the medication, and notify the health care provider
d. Explain to the client that this medication is contraindicated in glaucoma

CHAPTER 36
Reproductive Health Drugs

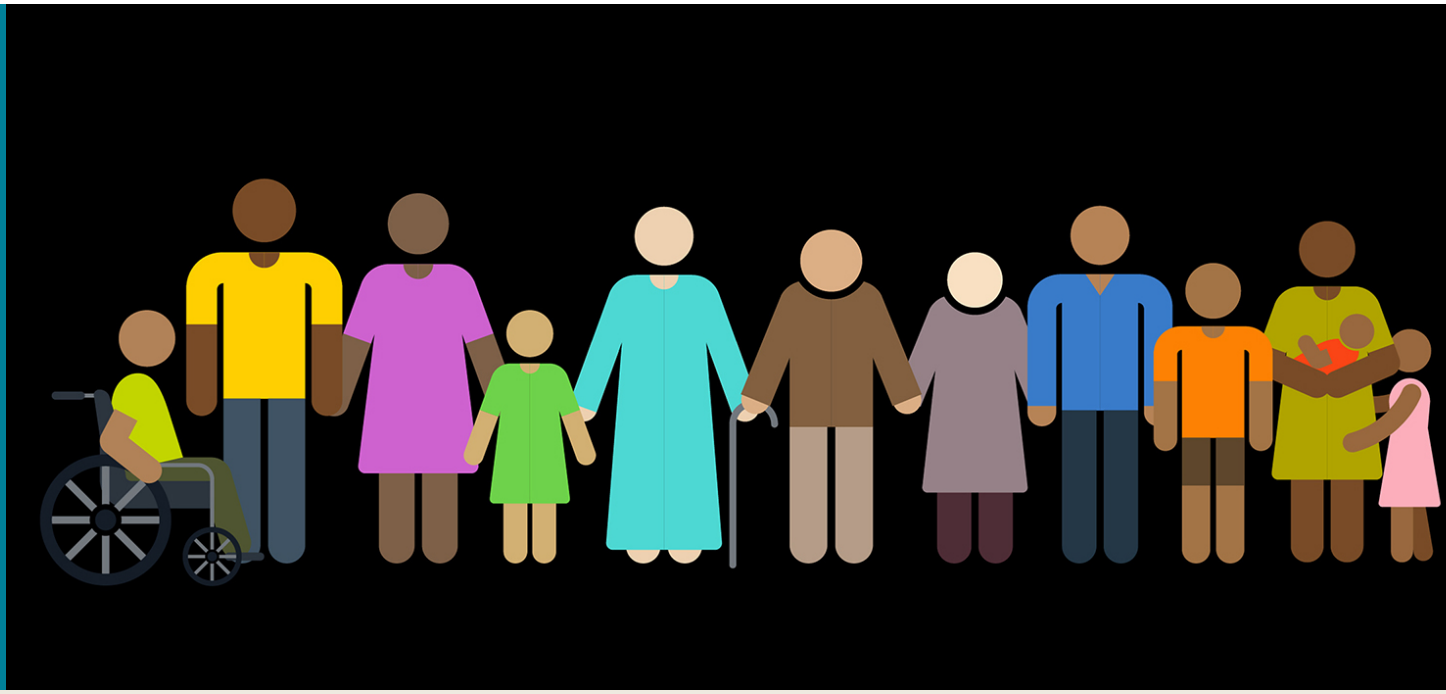


FIGURE 36.1 Supporting reproductive health involves caring for clients in a variety of life stages and with different gender expressions. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION This chapter focuses on the human reproductive systems and the medications used for various reproductive conditions. The chapter reviews the structure and function of the female and male reproductive systems and the hormones involved. Topics for the female reproductive system include menstruation, contraception, labor and delivery, postpartum, hormone replacement therapy, and menopause. Contraceptive methods are explored, including oral, topical, implanted, injected, and inserted, as well as indications, contraindications, and side effects of each. The chapter also examines medications used during the peripartum period. Additionally, it discusses menopause and drugs used to manage bone health. Topics for the male reproductive system include hormonal conditions, sexual performance, and andropause.

People often use the words “female” and “male” to describe two different concepts: our sense of gender identity and our biological sex as determined by our X/Y chromosomes, hormones, sex organs, and other physical characteristics. For some people, gender identity is different from biological sex, or their sex assigned at birth. In this chapter, “female” and “male” refer to biological sex only, and the typical reproductive anatomy of individuals with XX and XY chromosomes is discussed.

36.1 Review of the Female Reproductive System

LEARNING OUTCOMES

By the end of this section, you should be able to:

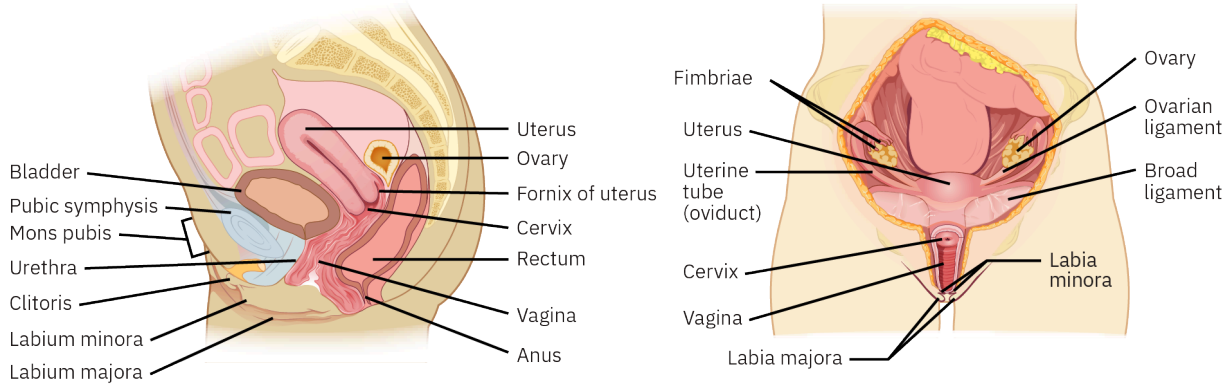
- 36.1.1 Describe the structure and function of the female reproductive system.
- 36.1.2 Discuss common conditions that affect the female reproductive system.

Structure and Function of the Female Reproductive System

The female reproductive system (also referred to as the ovarian reproductive system) is made up of internal and external organs (see Figure 36.2). The external parts, known also as the vulva (see Figure 36.3), include the labia majora, labia minora, clitoris, vaginal and urethral openings, and the mons pubis. The internal organs are the vagina, cervix, uterus, fallopian tubes, and ovaries (Hoare & Kahn, 2022; Netter, 2022).

The labia majora provide protection to the other external organs. The labia minora cover the openings to the urethra and the vagina. The clitoris is the junction of the labia minora and is the organ that allows sexual arousal to occur. The mons pubis is the small, rounded area made up of fat that sits just above the vulva. Pubic hair grows from the mons (Hoare & Kahn, 2022; Netter, 2022).

The uterus, or womb, is where a fertilized egg implants to develop into the fetus. If an egg is not fertilized and implanted, the uterus sheds its inner lining in the process usually known as menstruation or a period. The vagina is the birth canal, which connects the cervix, the lowest end of the uterus, to the outside of the body. During labor, the cervix gradually dilates to allow the fetus to enter the vagina. Strong contractions push the fetus through the vagina to the point where the fetus is born, meaning it has been delivered outside the body (Betts et al., 2023; Hoare & Kahn, 2022; Netter, 2022).



(a) Human female reproductive system: lateral view

(b) Human female reproductive system: anterior view

FIGURE 36.2 The internal ovarian reproductive system facilitates fertilization and fetal development during pregnancy, or menstruation if eggs are not fertilized or implanted. It is located within the pelvis and includes the vagina, cervix, uterus, fallopian tubes, and ovaries. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

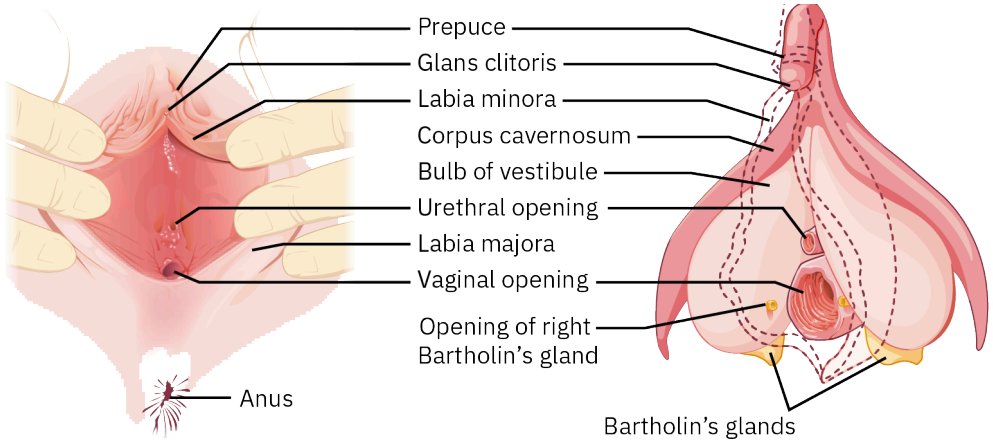


FIGURE 36.3 The external ovarian reproductive organs aid in reproduction and elimination. Known as the vulva, it includes the labia majora, labia minora, clitoris, vaginal and urethral openings, and the mons pubis. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Hormones

The major hormones affecting the female reproduction system are secreted from three locations in the body. The hypothalamus secretes a hormone known as the **gonadotropin-releasing hormone (GnRH)**. The anterior pituitary is stimulated by GnRH to secrete two hormones: **Follicle-stimulating hormone (FSH)** and **Luteinizing hormone (LH)**. Finally, the ovaries (gonads) themselves secrete **estrogen** and **progesterone** (gonadotropins) in response to FSH and LH released by the anterior pituitary. Each of these hormones is released during the monthly menstrual cycle, but in different amounts depending on the stage of the cycle. Estrogen and progesterone are gonadotropins.

GnRH is a critical hormone in the hypothalamic-pituitary-gonadal axis, acting as the central regulator. It is responsible for regulating the start of puberty, onset of menstrual cycle, development of sex characteristics, and ovulation. GnRH is also responsible for producing the gonadal sex hormones, LH and FSH (Casteel & Singh, 2023).

FSH and LH stimulate the development of ovarian follicles and the release of mature ova (eggs) from mature follicles. Additionally, FSH and LH prepare the body for pregnancy and support pregnancy until the time of delivery.

Estrogen is produced in three types: estradiol, estriol, and estrone. It initiates the development of the female genitalia and breast tissue and plays many roles during pregnancy to conserve energy for the fetus, increase metabolism, increase uterine motility, and other actions to prepare the body for pregnancy and delivery. Progesterone performs many of the same functions as estrogen does, to promote maturation of sex organs, prepare the body for pregnancy, and maintain a healthy uterine environment for development of the fetus.

The adrenal cortex secretes gonadocorticoids (gonadotropins), which are the sex hormones. Male hormones (androgens/testosterone) and female hormones (estrogen) are secreted in opposite sexes in very small amounts. However, they have minimal effect on the opposite sex (testosterone in females and estrogen in males) because hormones from the testes and ovaries override them. In menopause, androgen has more of a masculinization effect on females because the ovaries secrete less estrogen (Nassar, 2023).

Menstrual Cycle

The **menstrual cycle** refers to the monthly changes in hormones and reproductive organs that usually occurs on a 28-day cycle. The length of the cycle is different for each client and may be shorter or longer or even irregular for some individuals. The first menstrual cycle is known as **menarche** and generally begins around age 12, with some clients starting earlier and some not starting until their mid-teens. Each menstrual cycle begins with the first day of bleeding from the uterus. The bleeding is the discharge of blood and endometrial tissue, the lining of the uterus, which had been prepared for the implantation of a fertilized egg. Bleeding lasts around 5 days, though the length of time is individualized. Approximately 14 days after the first day of the cycle, ovulation occurs. The ovary releases an egg, and it travels through the fallopian tubes to the uterus to be fertilized and implanted. If no fertilization occurs,

the egg, along with the endometrial content, is expelled from the uterus, and the bleeding starts another menstrual cycle (McLaughlin, 2023; Rosner et al., 2022).

Hormones play a key role in the menstrual cycle through increased or decreased secretion from the hypothalamus, anterior pituitary, and ovaries. At the start of each cycle, the ovaries increase the production of estrogen until about day 14, when ovulation occurs; estrogen production then sharply decreases. During the second half of the cycle, estrogen secretion increases until about day 20 and then decreases to its lowest point when menstruation restarts, marking day 1 of a new cycle. Progesterone secretion, in contrast, is low until just before ovulation and then increases sharply, reaching a peak on about day 20. It then decreases gradually and remains low until the next ovulation at days 12–14 (McLaughlin, 2023; Rosner et al., 2022).

GnRH, LH, and FSH stimulate target cells (the cells that respond to a specific hormone) in the ovaries, causing the increased production of estrogen and progesterone. The hormone GnRH is secreted in bursts that vary in amplitude and frequency. The variations of amplitude and frequency also impact the start of other hormonal changes that regulate the menstrual cycle. Testosterone and progesterone decrease the frequency of GnRH bursts, whereas estrogens increase the frequency (Casteel & Singh, 2023). Additionally, LH and FSH increase the number and size of the target cells. Both LH and FSH secretion rise slightly at the start of the menstrual cycle, decrease, and then sharply increase immediately before day 14, or ovulation. They decrease significantly and rapidly after ovulation and remain steady until just before the start of a new cycle (McLaughlin, 2023; Rosner et al., 2022).

Figure 36.4 shows the phases of hormonal secretion.

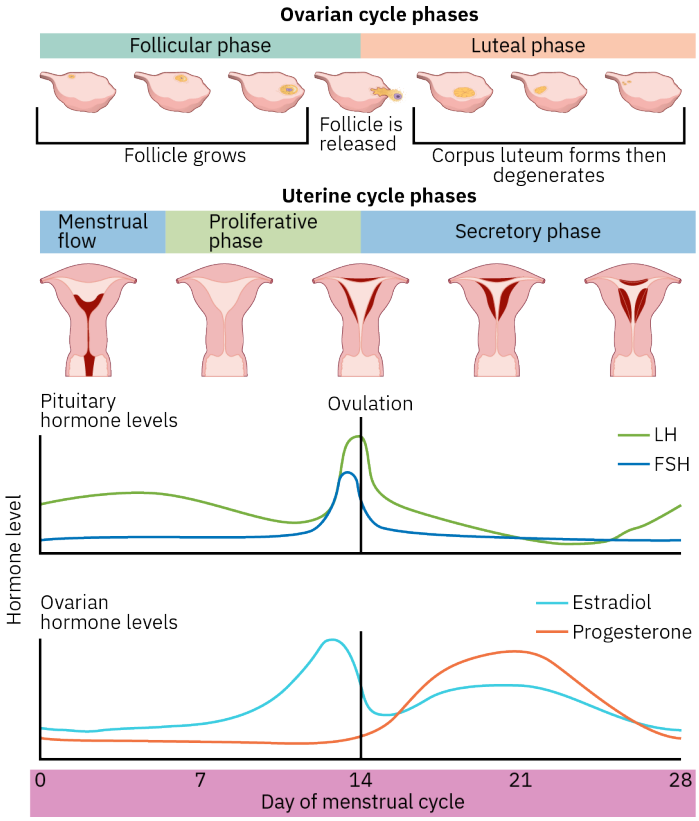


FIGURE 36.4 Rising and falling hormone levels result in progression of the ovarian and menstrual cycles. (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

LINK TO LEARNING

The Menstrual Cycle

Access multimedia content (https://openstax.org/books/pharmacology/pages/36-1-review-of-the-female-reproductive-system)

Dr. Paulien Moyaert is a Belgian nuclear medicine resident and science communicator. In this video, Dr. Moyaert explains the hormonal changes that occur during the menstrual cycle.

Pregnancy

Pregnancy means that an egg produced by the ovary has been released, fertilized by sperm, and implanted into the lining of the uterus and has begun to grow into a fetus. During pregnancy, the client will not have monthly menstrual cycles.

Three main groups of medications are related to pregnancy and will be discussed later in the chapter: contraceptives for clients who do not want to become pregnant, fertility medications for females who need help to become pregnant and maintain the pregnancy, and medications used during labor and delivery.

Menopause

Once a client has passed the age when they have regular monthly cycles, they have entered **perimenopause**. During perimenopause, the monthly menstrual cycle generally becomes irregular. A client may experience a missed cycle for one month and then have a period the following month. Cycles may occur closer together, the actual bleeding time may be shorter, and the amount of bleeding may decrease. **Menopause** is diagnosed once a client has not had any monthly cycles for 12 consecutive months (Peacock & Ketvertis, 2022; Mayo Clinic, 2023b; North American Menopause Society (NAMS) 2022 Hormone Therapy Position Statement Advisory Panel, 2022).

Menopause can occur in a client as early as their 30s until their mid-50s, with an average age of 51 years. Clients who experience menopause younger than age 40 are considered to have early menopause, usually the result of a genetic or chromosomal problem. Surgical menopause happens when the ovaries are surgically removed. Additionally, induced menopause may occur as the result of medications or radiation therapy that damages the ovaries. Whatever the reason for menopause, the signs and symptoms will be the same (Peacock & Ketvertis, 2022; Mayo Clinic, 2023b; NAMS 2022 Hormone Therapy Position Statement Advisory Panel, 2022).

During menopause, certain conditions develop that are the result of decreased hormones, specifically estrogen and progesterone. Vaginal dryness, hot flashes, night sweats, mood changes, weight gain, trouble sleeping, and thinning hair are what most clients experience during menopause. The intensity of each menopausal condition is individualized, so comparing one person's experience to another person's is not supportive to individual clients (Hariri & Rahman, 2023; NAMS 2022 Hormone Therapy Position Statement Advisory Panel, 2022; Mayo Clinic, 2023b; Peacock & Ketvertis, 2022).

One primary concern of menopause is the loss of bone mass, which can lead to fractures. This topic will be covered in more detail in the next section.

LINK TO LEARNING

Menopause

Access multimedia content (https://openstax.org/books/pharmacology/pages/36-1-review-of-the-female-reproductive-system)
Dr. Jen Gunter discusses what happens to the bodies of clients during menopause.

36.2 Hormonal, Contraception, and Infertility Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 36.2.1 Identify the characteristics of the hormonal therapy, contraception, and infertility drugs used to treat female reproductive disorders.
- 36.2.2 Explain the indications, actions, adverse reactions, and interactions of hormonal therapy, contraception, and infertility drugs used to treat female reproductive disorders.
- 36.2.3 Describe nursing implications of hormonal therapy, contraception, and infertility drugs used to treat female reproductive disorders.
- 36.2.4 Explain the client education related to contraception, hormonal therapy, and infertility drugs used to treat female reproductive disorders.

Hormonal Drugs

Hormonal drugs are derived from natural sources or manufactured to mimic the body's hormones. Hormonal drugs can be used for numerous conditions from contraception to menopause. They can replace the body's natural hormones when insufficient amounts are produced. They can also simulate or produce a state that is necessary for a specific reason. Contraception is an example in which hormonal drugs are used to create an environment that is not conducive to fertilization and implantation of an egg in the uterus.

Estrogens

Estrogen is produced in the body in four types: estrone (E1), estradiol (E2), estriol (E3), and estetrol (E4) (Hariri & Rehman, 2023). Indications for the use of estrogen include **hormone replacement therapy** (HRT) during menopause to relieve signs and symptoms such as vaginal dryness, hot flashes, mood swings, and painful intercourse. One type of estrogen, **estradiol**, can also be used as HRT for hypogonadism and ovarian failure (medical or physiological). Estradiol is available in a multitude of types and combinations, and dosages vary with the indication and use, the administration method, and its combined form (DailyMed, *Estradiol*, 2021; Hariri & Rahman, 2023).

Estrogens are administered in several ways. If administered orally, they are absorbed well from the gastrointestinal tract, metabolized by the liver, and excreted in urine. Depending on the dose, estrogens can inhibit or promote ovulation. Other positive effects include preservation of calcium and phosphorus and stimulation of bone growth.

Table 36.1 lists two forms of estrogen therapy that are synthetic but identical to the body's natural hormone and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Estradiol (Estrace, Divigel, Estraderm Transdermal)	*For postmenopausal symptoms:* *Oral:* Initial dose: 0.5–2 mg orally once daily. Adjust dose as necessary to control symptoms, using lowest effective dose. *Transdermal extended release (ER):* Initial dose: 0.0375–0.05 mg/24 hours applied topically twice weekly. Maintenance dose: 0.025–0.1 mg/24 hours applied topically twice weekly. *Transdermal (applied once weekly):* Available as 0.025 mg/day, 0.0375 mg/day, 0.05 mg/day, 0.06 mg/day, 0.075 mg/day, or 0.1 mg/day of estradiol. *Transdermal spray:* Initial dose: 1 spray (1.53 mg of estradiol) once daily in the morning to the forearm. Maintenance dose: 1–3 sprays once daily. *Vaginal cream:* 2–4 g daily administered vaginally with applicator for 1–2 weeks, then gradually reduce to half initial dosage for similar period. Maintenance dose of 1 g 1–3 times a week may be used. *Parenteral:* Estradiol cypionate (Depo-estradiol): 1–5 mg intramuscularly every 3–4 weeks. Estradiol valerate (Delestrogen): 10–20 mg intramuscularly every 4 weeks.
Estropipate (Improvera, Ortho-Est)	*For menopause:* 0.75–6 mg orally daily. *For female hypogonadism/primary ovarian failure:* 1.5–9 mg orally daily for the first 3 weeks of a theoretical cycle, followed by a rest period of 8–10 days. *For prevention of osteoporosis:* 0.75 mg orally for 25 days of a 31-day cycle per month.

TABLE 36.1 Drug Emphasis Table: Estrogen Derivatives and Synthetic Forms (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of estrogens are related mostly to the retention of fluids. Migraine headaches, bloating, weight gain, mood depression, stroke, and cardiovascular disease are known adverse reactions and can be life-threatening.

Contraindications for estrogens include hormone-positive breast cancer, undiagnosed uterine bleeding, and active or history of thrombophlebitis or thromboembolism. Pregnancy and breastfeeding are also contraindications because estrogens cross the placenta and enter breast milk. Estrogens must be used cautiously in conditions that are affected or exacerbated by fluid retention, such as migraine headaches with an aura, renal or cardiac dysfunction, and hypertension. Obesity and age greater than 35 are circumstances when estrogens should be used cautiously, if at all.

Table 36.2 is a drug prototype table for estrogens featuring conjugated estrogen. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Estrogen (hormone) **Mechanism of Action** Replaces estrogen normally produced by the body	**Drug Dosage** *HRT:* 0.3–0.625 mg/day orally (25 days on and 5 days off). *Female hypogonadism:* 0.3 mg or 0.625 mg daily orally (25 days on and 5 days off). *Female castration or primary ovarian failure:* 1.25 mg orally daily (25 days on and 5 days off). *Palliative treatment of breast cancer:* 10 mg orally 3 times daily. *Palliative treatment of prostate cancer:* 1.25–2.5 mg orally 3 times daily.
Indications To replace hormones during menopause To manage primary ovarian failure To manage abnormal uterine bleeding related to hormone imbalance To relieve symptoms of low estrogen in young females who do not produce enough estrogen naturally (hypogonadism) **Therapeutic Effects** Decreases symptoms of menopause (vaginal dryness, hot flashes, night sweats, mood changes, weight gain, trouble sleeping, and thinning hair) Palliative treatment in advanced prostate cancer or male breast cancer	**Drug Interactions** Ketoconazole Barbiturates Carbamazepine Phenytoin Penicillin Tetracyclines Rifampin St. John's wort False unicorn root Red clover Wild yams **Food Interactions** Grapefruit and grapefruit juice
Adverse Effects Weight gain Nausea Bloating Headaches Photosensitivity Intolerance of contact lenses Breast tenderness Depression Increased risk of stroke Heart attack Deep vein thrombosis and other thrombotic events Breast and ovarian cancer	**Contraindications** Undiagnosed abnormal uterine bleeding Female breast cancer Active or history of thrombophlebitis or thromboembolic problems (deep vein thrombosis, pulmonary embolism) Active or history of cardiovascular disease or arterial thromboembolic diseases (stroke, heart attack) Pregnancy Estrogen-dependent neoplasia Known anaphylactic reaction, angioedema, hypersensitivity Hepatic impairment or disease Protein C, protein S, or antithrombin deficiency, or other known thrombophilic disorders Caution: Older than 35 years Smoking

TABLE 36.2 **Drug Prototype Table: Conjugated Estrogen** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Estrogen

Estrogen (both estrogen alone or estrogen-progestin combinations) can significantly increase the risk of

cardiovascular events such as stroke and heart attack in postmenopausal clients.

It can significantly increase the risk of invasive breast cancer in postmenopausal clients.

It should not be used to prevent dementia as part of hormone replacement therapy.

Progestins

Progestins include progesterone and its derivatives. They can function as both a stimulant and an inhibitor to manage the secretion of pituitary gonadotropins. One of the properties of progestins is their ability to prevent follicular maturation and ovulation. They accomplish this by inhibiting the secretion of pituitary gonadotropins and decreasing LH secretion. Progestins thicken cervical mucus, which hinders sperm migration and changes the endometrium to decrease the likelihood that an egg can be implanted. These properties make progestins an excellent contraceptive medication. Progestins are metabolized by the liver and excreted in urine.

Progesterone is used for several reasons. It can be added to estrogen in postmenopausal HRT to reduce the risk of endometrial cancer. It is also used for amenorrhea and for dysfunctional uterine bleeding. It can be administered orally, intramuscularly, intrauterine, and as a gel, depending on the intended effect of the drug. Progesterone dosage for HRT varies, as does the number of days it is used per month.

Desogestrel, drospirenone, medroxyprogesterone, norethindrone, and levonorgestrel are progestins. Desogestrel and drospirenone are used only in combination form for contraception.

Table 36.3 lists common progestins and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Desogestrel/ethinyl estradiol (Cyclessa, Mircette)	150 mcg of desogestrel/30 mcg of ethinyl estradiol orally once daily (on specific days as instructed; inactive tablets are included and should be taken as directed).
Drospirenone/ethinyl estradiol (Syeda, Yasmin, YAZ)	3 mg of drospirenone/0.02 or 0.03 mg of ethinyl estradiol orally once daily (as per instructions depending on specific brand name or package; inactive tablets are included and should be taken as directed).
Medroxyprogesterone (Depo-Provera, Provera)	*Intramuscular:* 150 mg/mL every 3 months. *Subcutaneous:* 104 mg/0.65 mL every 3 months.
Norethindrone (Camila, Ortho Micronor)	2.5–10 mg orally daily.
Levonorgestrel (Alesse, Introvale, Lessina)	1.5 mg orally as soon as possible within 72 hours of unprotected sexual intercourse or known or suspected contraceptive failure.

TABLE 36.3 Drug Emphasis Table: Progestins (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects, contraindications, and precautions for progesterone are similar to those of estrogen and include weight gain, nausea, bloating, headaches, visual disturbances, rash, and acne. Contraindications for progestin are hypersensitivity, pregnancy/lactation, history of thrombotic events, sexually transmitted disease (STD), pelvic inflammatory disease, endometriosis, undiagnosed uterine bleeding, cardiac/renal/liver disease, and hormone-sensitive cancers. Caution should be used with clients who have any condition that can be affected by fluid retention (migraine headache, cardiac/renal disease, seizure disorder), diabetes, hyperlipidemia, or clinical depression.

Table 36.4 is a drug prototype table for progestins featuring norethindrone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Progestin (hormone) **Mechanism of Action** Inhibits secretion of FSH and LH Inhibits follicle maturation and ovulation	**Drug Dosage** 2.5–10 mg orally daily.
Indications To prevent pregnancy (contraceptive) To treat primary and secondary amenorrhea To treat functional uterine bleeding To treat female hypogonadism **Therapeutic Effects** Palliative treatment of certain cancers (inoperable breast, prostate) Decreases symptoms of menopause Delays progression of osteoporosis	**Drug Interactions** Barbiturates Carbamazepine Phenytoin Penicillin Tetracyclines Rifampin St. John's wort False unicorn root Red clover Wild yams **Food Interactions** Grapefruit/grapefruit juice
Adverse Effects Weight gain Nausea Bloating Headaches Visual disturbances Rash Acne Breakthrough bleeding/spotting Fluid retention/edema Chloasma (hyperpigmentation of skin) Alopecia Venous thromboembolism	**Contraindications** Hypersensitivity Pregnancy/lactation History of thrombotic events STD Pelvic inflammatory disease Endometriosis Undiagnosed uterine bleeding Cardiac/renal/liver disease Hormone-sensitive cancers Caution: Any condition that can be affected by fluid retention (migraine headache, cardiac/renal disease, seizure disorder) Diabetes Hyperlipidemia Clinical depression

TABLE 36.4 **Drug Prototype Table: Norethindrone** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Progesterone

In combination with estrogen, progesterone can significantly increase the risk of ovarian cancer.

Progesterone should not be used to prevent cardiovascular disease in postmenopausal clients.

LINK TO LEARNING

Hormone Replacement Therapy (https://openstax.org/r/menopauseindepth)

Hormone replacement therapy was once commonly used to treat common menopausal symptoms, but large

clinical trials have shown health risks. The Mayo Clinic discusses hormone replacement therapy and whether it is right for certain clients.

Contraceptives

Contraceptives are a group of medications, generally natural or synthetic hormone preparations, used to prevent pregnancy. Hormonal contraceptive medications work at distinct stages within the female (ovarian) reproductive system and use a variety of methods to interrupt the normal cycle of hormone release, egg fertilization, and/or implantation. Hormonal contraceptives can be oral, topical, vaginal, injectable, or implantable.

One important fact concerning all contraceptives, except male and female condoms, is that they do not prevent **sexually transmitted infections** (STIs). Therefore, client education about this topic is crucial. Another major consideration about contraceptives is that none of them is 100% effective in preventing pregnancy. There is a risk that sexual intercourse, even with the use of contraceptives, can lead to pregnancy (Britton et al., 2020).

Synthetic forms of estrogen and progestin are the hormones used in contraceptive drugs. These drugs contain either an estrogen-progestin combination or progestin alone. Estrogen works by the negative feedback loop to decrease the secretion of LH and FSH from the anterior pituitary gland. With lower levels of LH and FSH, a dominant follicle will not develop, and a mature egg will not be released from the follicle (Britton et al., 2020; Casey, 2022; Cooper et al., 2020).

Progestin thickens the cervical mucous and prevents sperm from reaching the egg. It also changes the endometrium so that the environment of the uterus is less favorable for egg implantation. Refer to the previous section regarding hormones for specific information about estrogen and progestin.

The combination oral contraceptives (COC) and progestin-only contraceptives (POP) make up two types of oral contraceptive pills. The third type is a continuous or extended-use pill, which means the pills are taken without any pause for an indefinite time. This contraceptive regimen allows for increased ovulation suppression and medication adherence, is more satisfactory for the user, and decreases both scheduled and breakthrough bleeding over time (Britton et al., 2020; Casey, 2022; Cooper et al., 2020).

CLINICAL TIP

Dealing with Side Effects of Birth Control Methods

The most frequent side effects of all birth control methods are nausea and breakthrough bleeding. Instructing the client to take the medication before going to bed is one of the best ways to manage nausea so that the client is asleep when the worst of the nausea occurs. Eating small meals frequently, avoiding spicy and greasy foods, and drinking ginger ale or clear liquids are other ways to alleviate nausea. The nausea should go away after about 3 months.

Breakthrough bleeding can be frustrating to the client. However, this should also subside after 3 months. Some clients may have only spotting and some may have times of heavy bleeding other than their period (if contraceptive method allows for monthly cycle to continue).

There is no way to determine which client will have which side effects. Every individual's experience is different. The body is adjusting to new levels of hormones, and this process takes about 3 months. Emotional support to the client is also important. Some clients may need to try more than one contraceptive pill or method to find the best fit for their situation.

Oral and Injectable Contraceptives

Oral contraceptives are pills that contain either a combination of estrogen and progestin or progestin alone. Oral contraceptives are prescribed based on a client's medical history, needs, and risk factors. **Combined oral contraceptives (COCs)** contain estrogen and progestin in varying dosages. The type of progestin varies with each COC depending on the individual client's needs and medical status. There are three different categories of COCs. Monophasic contraceptive pills contain a fixed ratio of estrogen and progestin. Biphasic COCs contain a fixed dose of estrogen with a varying dose of progestin. Triphasic COCs contain low doses of both estrogen and progestin with a

varying dose of estrogen (Britton et al., 2020; Casey, 2022; Mayo Clinic, 2023a; Cooper et al., 2020).

Injectable contraceptives are hormones that are injected, usually intramuscularly, at specific intervals to provide the same birth control protection as oral contraceptives (Britton et al., 2020; Casey, 2022; Cooper et al., 2020).

Table 36.5 lists common forms of COCs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Monophasics	
Estradiol levonorgestrel (Aviane)	20 mcg estradiol/0.10 mg levonorgestrel orally (21 active pills and 7 inactive pills).
Ethinyl estradiol desogestrel (Apri 28)	30 mcg ethinyl estradiol/0.15 mg desogestrel orally (21 active pills and 7 inactive pills).
Biphasics	
Levonorgestrel and ethinyl estradiol (Seasonique)	13-week supply of tablets: • 84 blue-green tablets, each containing 0.15 mg of levonorgestrel and 0.03 mg ethinyl estradiol. • 7 yellow tablets each containing 0.01 mg of ethinyl estradiol.
Triphasics	
Desogestrel/ethinyl estradiol (Mircette)	Days 1–21: 0.02 mg ethinyl estradiol/0.15 mg desogestrel (21 tablets). Day 22–23: Inactive tablets (2 tablets). Day 24–28: 0.01 mg ethinyl estradiol (5 tablets).

TABLE 36.5 **Drug Emphasis Table: COCs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Progestin-only contraceptives are used when estrogen is not appropriate for the client's situation. For instance, the client may have significant risk factors such as obesity, smoking, hypertension, and age over 35 years. These are also commonly used by clients who are breastfeeding, as they have less effect on the breast milk supply than oral contraceptives containing estrogen. Medroxyprogesterone, norethindrone, and levonorgestrel are progestin-only contraceptives. The injectable contraceptive medroxyprogesterone is administered intramuscularly or subcutaneously (Britton et al., 2020; Casey, 2022; Cooper et al., 2020).

Table 36.6 lists common progestin-only contraceptives and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Medroxyprogesterone (Provera, Depo-Provera)	*Amenorrhea:* 5–10 mg orally daily for 5–10 days. *Contraception:* 150 mg/1 mL intramuscularly every 3 months; 104 mg/0.65 mL subcutaneously. *Adjunct cancer treatment (endometrial or renal carcinoma):* 400–1000 mg intramuscularly weekly. May decrease to 400 mg intramuscularly monthly depending on client response. Used only as adjunctive and palliative treatment for advanced inoperable cases.
Norethindrone acetate (Aygestin, Finzala)	*Amenorrhea:* 2.5–10 mg Aygestin orally daily for 5–10 days. *Contraception:* 24 chewable active Finzala tablets with 1 mg norethindrone acetate/20 mcg ethinyl estradiol along with 4 nonhormonal placebo tablets. 1 tablet orally daily.
Levonorgestrel (Plan B One-Step)	*Contraception:* 1.5 mg orally as soon as possible within 72 hours of unprotected sexual intercourse or contraceptive failure.
Ulipristal acetate (Ella)	*Contraception:* 30 mg orally as soon as possible within 5 days (120 hours) after unprotected sex or contraceptive failure.

TABLE 36.6 **Drug Emphasis Table: Progestin-Only Contraceptives** (source: https://dailymed.nlm.nih.gov/dailymed/)

LINK TO LEARNING

Contraceptive Options (https://openstax.org/r/womenshealth)

Birth Control Methods is a client education site that discusses birth control options and resources for obtaining them.

Intrauterine and Implanted Contraceptives

In addition to oral and injectable contraceptives, **intrauterine devices (IUDs)** and **implanted contraceptive devices** are available. The advantages to these forms of contraception are their long-term effects and ease of use. They do not require remembering to take daily pills or scheduling appointments for injections. However, they do have side effects, like any hormonal medication. Additionally, because they are inserted into the body, risks of infection and migration (moving) or dislodgement of the devices exist (Andersen & Spanfeller, 2022; Britton et al., 2020; Casey, 2022; Madden, 2023).

IUDs have become the most commonly used contraceptive method in the world and are among the most effective types of contraceptives. IUDs are small T-shaped devices that are placed inside the uterus via the cervix. Five types of IUDs are used in the United States. Four of them are hormonal. They release small amounts of progestin (levonorgestrel) into the body. They also have a positive effect of making monthly periods lighter. Further, these IUDs may decrease the risk of ovarian, endometrial, and cervical cancers (Andersen & Spanfeller, 2022; Casey, 2022; Madden, 2023).

The fifth type is copper. It works by stimulating the body's immune response, creating an unfavorable uterine environment for the sperm, and preventing pregnancy. It may initially increase bleeding with periods and between periods; however, the bleeding should lessen to an acceptable level. Hormonal IUDs can last for 3–8 years, depending on the specific hormone and dose, and the copper type lasts for 10 years (Andersen & Spanfeller, 2022; Britton et al., 2020; Casey, 2022; Madden, 2023).

Another type of birth control method is the implanted device. The device comes as a single soft, radiopaque, flexible implant (4 cm in length × 2 mm in diameter) that contains 68 mg etonogestrel, 15 mg barium sulfate, and 0.1 mg magnesium stearate. It comes with the insertion device in the package. The contraceptive is implanted under the skin of the inner upper arm. It has the same action, use, contraindications, and side effects as any other contraceptive containing levonorgestrel. The primary risk is infection or dislodgement of the implant. This device lasts for 3 years and is a highly effective contraceptive method (Britton et al., 2020; Casey, 2022; DailyMed, *Nexplanon*, 2022).

Table 36.7 lists the four hormonal IUD types and dosing for adult clients.

Drug	Routes and Dosage Ranges
Levonorgestrel (Kyleena Liletta Mirena Skyla)	 Intrauterine 19.5 mg. Intrauterine 52 mg (20.1 mcg/day). Intrauterine 52 mg (20 mcg/day). Intrauterine 13.5 mg.

TABLE 36.7 Drug Emphasis Table: Hormonal IUDs (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Contraindications include active STI or recent pelvic infection, pregnancy, cancer of the cervix or uterus, or unexplained vaginal bleeding. Hormonal IUDs should not be used by clients who have had breast cancer.

Side effects include bleeding and spotting as the uterus adjusts to the IUD. Other adverse effects include abdominal pain, endometriosis, pelvic inflammatory disease (PID), and expulsion of the IUD. Extremely rare is the possibility that an IUD may cause uterine perforation.

For a copper IUD, the bleeding and spotting may last up to 6 months. The insertion of the IUD may be uncomfortable, and the client may experience some cramping and backache for a day or two after the procedure. The pain can be managed using ibuprofen or acetaminophen and heating pads. Other side effects include nausea,

cramping, ovarian cysts, and mood changes. The most concerning complications of all IUDs are infection, expulsion, or perforation; however, the risk for these complications is extremely low (Andersen & Spanfeller, 2022; Britton et al., 2020; Casey, 2022; Madden, 2023).

Other Contraceptive Methods

Two other hormonal contraceptive methods are a transdermal patch and a vaginal ring. The patch contains an estrogen–progestin combination and is applied weekly for 3 weeks and left off for 1 week. The vaginal ring also contains a combination of estrogen–progestin and is inserted once and left in place for 3 weeks. The ring is removed for 1 week before a new ring is inserted. Both methods are based on a 4-week cycle (Britton et al., 2020; Casey, 2022).

In 2018 the FDA approved a new vaginal ring that is reused for a year (Center for Devices and Radiological Health, 2018). It is used according to the same cycle of 3 weeks in place and 1 week out. The difference is that between cycles it can be washed and stored and then reused.

Specific client teaching for the vaginal ring includes properly placing and removing the ring and properly disposing of the monthly ring or cleaning and storage of the yearly ring. If the ring is removed for more than 3 hours, clients should be advised to use a backup contraceptive method concurrently for 7 days (Britton et al., 2020; Casey, 2022).

Client teaching for the patch includes correct opening of the package; placing the patch on clean, dry skin on the buttocks, upper outer arm, lower abdomen, or upper body; pressing it firmly for 10 seconds; and not placing the patch on the breasts (Britton et al., 2020; Casey, 2022).

All contraceptive drugs, regardless of form, are derived from the hormones estrogen and progestin. Refer to Table 36.1 and Table 36.3 for information related to mechanism of action, indication, therapeutic effects, side effects, contraindications, and food and drug interactions.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Susan Lopez is a 34-year-old female who presents to the public health department for counseling regarding contraception. She is planning to be married, and she and her fiancé do not want children. Susan has been sexually active with three male partners including her fiancé. She has always insisted that the partners use condoms.

Social History

Tobacco use: Smokes e-cigarettes daily. Formerly smoked regular cigarettes, 1/2 pack per day. Total time smoking is 10 years.
Alcohol use: Occasional social drink, usually wine
Sexually active

Current Medications

None

Vital Signs		Physical Examination
Temperature:	98.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Within normal limits • *Cardiovascular:* S1, S2 noted • *Respiratory:* Clear bilaterally • *GI:* Abdomen soft, nontender, nondistended • *GU:* Reports normal urine output • *Neurological:* Within normal limits; reports history of migraine headaches • *Integumentary:* Skin appropriate for age • *Gynecological:* Normal exam; urine pregnancy test negative; no reports of signs or symptoms of sexually transmitted infection (STI) and none noted during exam
Blood pressure:	128/78 mm Hg	
Heart rate:	74 beats/min	
Respiratory rate:	16 breaths/min	
Height:	5'3"	
Weight:	152 lb	

TABLE 36.8

1. The nurse completes the initial assessment for Susan. Which finding is the most important regarding counseling about contraceptive medications?
    a. Weight and BMI
    b. Sexual history
    c. Smoking
    d. Migraine headache

2. After discussing all the options for contraception with Susan and considering that Susan does not want children, which method do Susan and the nurse think may be the best for her?
    a. Oral, daily combination hormone pill
    b. Depo-Provera injection once every 3 months
    c. Hormonal IUD
    d. Copper IUD

Initiating Contraceptives

The oral and transdermal methods can be initiated using a first-day start method, a quick start method, or a Sunday start method. All are equally effective. The **first-day start method** means the client starts the contraceptive on day 1 of their menstrual cycle and continues as directed. The **quick start method** means that the client starts the contraceptive immediately, regardless of the timing of their menstrual period. This is week one. The individual continues to take the pills or apply the patch as directed. One advantage of the quick start method is that the client can begin taking the medication the day they receive the medication. The **Sunday start method** means the client will start using the contraceptive on the first Sunday following the start date of their period. Then the client continues to take the pills or apply the patch as directed. A disadvantage of the Sunday start method is that clients may forget to start on the correct date and then must wait until after their next period to begin taking the medication (Britton et al., 2020; Casey, 2022; Cooper et al., 2020).

LINK TO LEARNING

How to Provide Quality Counseling for Contraception (https://openstax.org/r/acog)

This position statement from American College of Obstetricians and Gynecologists provides information about client-centered contraceptive counseling. It highlights the importance of recognizing health disparities and bias that can occur when counseling clients on contraceptive use and recommends a shared decision-making approach through client-centered contraceptive counseling.

Infertility Drugs

Infertility drugs constitute a highly specialized class of drugs. The content in this chapter is intended to give the reader an introduction to the topic. Infertility can occur for numerous reasons that are beyond the scope of this

chapter to detail. Some causes of infertility are related to impaired hormone secretion from the reproductive system and the thyroid. Other causes include blockages or conditions that require surgical intervention to resolve. This chapter will cover only the drugs used to promote fertility.

Some clients cannot become pregnant without exogenous treatment, meaning they will need medications administered to assist their body's reproductive system to ovulate and for the egg to mature. Some medications directly stimulate the follicles and ovulation; others stimulate the hypothalamus to increase the secretion of FSH and LH, which then lead to follicle and ovary development and maturation.

These medications are typically used only for clients who have functioning ovaries and who have been unable to become pregnant after at least 1 year of trying. However, if a client is over age 35, fertility drugs are generally used after 6 months of trying. The other purpose of infertility drugs is for people who want multiple follicles developing in order to harvest ova for in vitro fertilization.

One important aspect of fertility treatment is the complex schedule for taking each medication and when intercourse should take place to increase the chance of egg fertilization. Additionally, provider appointments may not be easy to facilitate if the client lives a distance from the clinic or is limited by their personal situation in scheduling appointments at the clinic. Further, if the client is self-administering injections, they will need instructions and supplies.

Table 36.9 lists common infertility drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Clomiphene (Clomid)	50–100 mg orally daily. Timing and length of therapy are dependent on individual client situations.
Cetrorelix acetate (Cetrotide)	0.25 mg subcutaneously once daily during the early- to mid-follicular phase. 0.25 mg subcutaneously on either stimulation day 5 (morning or evening) or day 6 (morning) and continued daily until the day of human chorionic gonadotropin (hCG) administration.
Human chorionic gonadotropin (hCG) (Ovidrel)	5000–10,000 USP (U.S.) units intramuscularly 1 day following the last dose of menotropin. 250 mcg subcutaneously 1 day following the last dose of the follicle-stimulating agent.
Follitropin (Follistim AQ, Gonal-F, Gonal-F RFF)	*Follistim AQ:* 50 international units subcutaneously daily for at least the first 7 days; dosage adjusted weekly based on ovarian response. *Gonal-F:* Dosing depends on individual situation.
Menotropin (Menopur)	*Initial dose*: 225 international units subcutaneously on cycle day 2 or 3; adjust dose after 5 days and subsequent adjustments made per ovarian response.

TABLE 36.9 Drug Emphasis Table: Infertility Drugs (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of infertility drugs include a significant risk of multiple births and birth defects. Ovarian overstimulation is another side effect that is manifested by abdominal pain, distention, ascites (fluid accumulation in the abdomen), and pleural effusion. Headache, fluid retention, ovarian enlargement, uterine bleeding, nausea, and fever are additional side effects.

Infertility drugs are contraindicated when the client has primary ovarian failure, thyroid or adrenal dysfunction, ovarian cysts, or idiopathic uterine bleeding or is pregnant. Clients with respiratory issues or who are breastfeeding should use caution before deciding to take fertility medications.

Table 36.10 is a drug prototype table for infertility drugs featuring clomiphene. Clomiphene is a selective estrogen receptor modulator (SERM) with both estrogen antagonist and agonist effects that increase gonadotropin release as well as increase production of FSH and LS. The ultimate effect is ovarian follicular growth (Carson & Kallen, 2021). The table lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Infertility drug **Mechanism of Action** Stimulates ovarian reproductive system	**Drug Dosage** 50–100 mg orally daily. Timing and length of therapy are dependent on individual client situations.
Indications Treatment of ovulatory dysfunction in clients desiring pregnancy **Therapeutic Effects** Creates reproductive environment conducive to pregnancy	**Drug Interactions** No significant interactions **Food Interactions** Alcohol
Adverse Effects Ovarian hyperstimulation syndrome (OHSS) Ovarian enlargement Vasomotor flushes Abdominal-pelvic discomfort/distention/bloating Nausea and vomiting Breast discomfort Visual symptoms (blurred vision, lights, floaters, waves, unspecified visual complaints, photophobia, diplopia, scotomata, phosphenes) Headache Abnormal uterine bleeding Intermenstrual spotting, menorrhagia Significant risk of multiple births and birth defects	**Contraindications** Hypersensitivity Pregnancy Uncontrolled thyroid or adrenal dysfunction Organic intracranial lesion such as pituitary tumor Abnormal uterine bleeding Ovarian cysts Liver disease

TABLE 36.10 **Drug Prototype Table: Clomiphene** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking hormone therapy, contraceptives, or infertility drugs:

- Assess client's baseline health status to include medical history, physical exam, and complete medication history, including herbal remedies and over-the-counter (OTC) medications.
- Assess for factors that increase the client's risk of adverse effects including personal and family history of cardiovascular disease (myocardial infarction, cerebral vascular accident, hypertension, and thrombotic events including venous thromboembolism and pulmonary embolism).
- Assess smoking history and alcohol use.
- Assess pregnancy and lactation status (for contraceptive use).
- Assess for presence of or risk of sexually transmitted infection (for clients obtaining contraception).
- Assess client's emotional status and support system.
- Identify any factors that may affect the client's ability to adhere to the medication regime.
- Obtain serum and urine specimens as ordered.
- Assist with gynecological exam as needed.
- Assess baseline sexual development for prepubescent clients taking hormone therapy.
- Obtain baseline vital signs and weight and monitor at each follow-up appointment.
- Assess client's understanding of the drugs to be used—actions, side effects, contraindications, administration method, and schedule–and provide instruction as indicated.
- Provide information in a calm, supportive, nonjudgmental manner.
- Assist the client with their choice of contraceptive method according to individual needs and preferences.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a hormone therapy, contraceptive, or infertility drug should:

- Understand the purpose, effect, and side effects of the medication(s).
- Be able to follow the drug schedule (daily, cyclical).
- Be able to self-administer drug as ordered (topical, transdermal, oral, injection).
- Verbalize the importance of taking medications at the same time and what to do for missed doses.
- For clients using contraceptives, understand the need for using a barrier or nonhormonal birth control method to prevent pregnancy when beginning contraception and any time 3 or more consecutive doses of oral contraceptive are missed. The alternate method should generally be used for a minimum of 7 days.
- For clients using contraception, understand that it does not protect against STIs, so barrier methods (condoms) must be used to prevent the spread of infections.
- For clients with transdermal patches or vaginal rings, understand what to do when they are dislodged or removed during the active time.
- For clients with an implanted contraceptive device, understand the potential complications of infection and migration of the device.
- Report problems such as breakthrough bleeding and any intolerable side effects to the health care provider.
- Avoid prolonged exposure to sunlight (hormone therapy).
- Recognize any change in vision and/or problems with contact lenses (hormone therapy).
- Initiate smoking cessation in the manner most suited to the client (medication, support group, etc.).
- Clients taking infertility medications should understand the possibility of multiple births.
- Dispose of any sharps in a safe manner.
- Clients taking infertility medications should be able to follow the schedule for sexual intercourse as determined to maximize chances for pregnancy success.
- Report new health problems to the health care provider in a timely manner.
- Notify the health care provider immediately of chest pain and/or shortness of breath; any pain, swelling, and/or redness in calves; severe headache; signs and symptoms of stroke; and any significant change in mood (depression).
- Notify the health care provider before taking any new medication or OTC/herbal remedies.
- Maintain follow-up appointments.

The client taking a hormone therapy, contraceptive, or infertility drug *should not:*

- Smoke because of the increased risk of blood clots (hormone therapy, contraceptives).
- Discontinue or alter the dose of the medication without consulting with their health care provider.

36.3 Uterine Motility Drugs and Lactation Considerations

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 36.3.1 Identify the characteristics of uterine motility drugs used during pregnancy and labor.
- 36.3.2 Explain the indications, actions, contraindications, and adverse reactions of uterine motility drugs used during pregnancy and labor.
- 36.3.3 Describe nursing implications for uterine motility drugs used during pregnancy and labor.
- 36.3.4 Explain the client education related to uterine motility drugs used during pregnancy and labor.
- 36.3.5 Briefly discuss maternal and fetal health considerations when using medications during pregnancy, labor, and delivery.
- 36.3.6 Briefly describe nursing implications and client education regarding medication use while breastfeeding.

Uterine motility drugs are used during labor to stimulate contractions (**oxytocics**) or to induce abortion (**abortifacients**). Other medications (**tocolytics**), such as terbutaline, are used to delay contraction in the event of premature labor.

Lactation is the secretion of breast milk by the mammary glands. Some medications can pass from breast milk to the infant. Thus, when the lactating client must take medications, consideration must be given to the possible harmful effects on the infant. Because this content is highly specialized and used only in maternal health, this section will cover only basic information.

Uterine Motility Drugs

Uterine motility drugs affect the movement (contractions) of the uterus. Motility drugs may either increase or decrease uterine contractions, depending on the client's specific situation. Fetal distress, abnormal fetal presentation, fetal demise, and maternal hemorrhage might be reasons to increase uterine contractions and facilitate delivery. On the other hand, premature labor may be a reason to slow uterine contractions. Generally, these medications are administered in an acute-care setting with monitoring equipment available.

Oxytocics

Oxytocics are used to induce and increase uterine contractions during labor. The two drugs in this category are methylergonovine and oxytocin. These drugs are administered in labor and delivery or postpartum units in a medical facility where the client can be monitored closely.

Methylergonovine is administered IM or via IV immediately after delivery and then orally for up to 1 week as needed. Methylergonovine works directly on the uterine smooth muscle to prevent postpartum hemorrhage. It also helps with uterine involution, the process whereby the uterus gradually resumes its prepartum size and weight. The IM dose is 1 mL (0.2 mg) after delivery of the anterior shoulder, after delivery of the placenta, or during the puerperium (several weeks after childbirth). Dosage may be repeated as required at intervals of 2–4 hours. The IV dose is 1 mL (0.2 mg) administered slowly over a period of no less than 60 seconds (DailyMed, *Methylergonovine,* 2020).

Oxytocin is administered by intravenous infusion starting at 1–2 mU/minute and gradually increased in increments of no more than 1–2 mU/minute until a normal labor contraction pattern is established. Oxytocin works by exerting a selective action on the smooth musculature of the uterus, which stimulates rhythmic contractions of the uterus, increases the frequency of existing contractions, and improves muscle tone of the uterus. It can be used to facilitate labor contractions as well as to prevent postpartum hemorrhage.

Table 36.11 lists common oxytocics with typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Methylergonovine (Methergine)	1 mL (0.2 mg) intramuscularly or intravenously (IV) (IV dose administered slowly over a period of no less than 60 seconds).
Oxytocin (Pitocin)	*Continuous infusion:* 1 mL (10 units/mL) combined with 1000 mL of an isotonic diluent such as lactated Ringer's solution. *Initial dose:* No more than 1–2 mU/minute; may be gradually increased in increments of no more than 1–2 mU/minute until normal labor contraction pattern established. *To control postpartum bleeding:* 10–40 units added to 1000 mL of a nonhydrating diluent. Rate adjusted as necessary to control uterine atony. 1 mL (10 units) of oxytocin intramuscularly after delivery of placenta.

TABLE 36.11 Drug Emphasis Table: Oxytocics (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Methylergonovine is contraindicated or used cautiously in clients who have coronary artery disease, diabetes, or hypercholesterolemia because it may increase the risk for more serious side effects. Kidney and liver disease are also conditions that may require caution when using methylergonovine because of delayed metabolism and excretion of the drug. Pregnancy, hypertension, and toxemia are contraindications for the drug. One notable drug–food interaction is grapefruit and grapefruit juice (DailyMed, *Methylergonovine*, 2020).

Side effects include worsening of cardiovascular disease, diabetes, hypercholesterolemia, abdominal pain, headache, and increased blood pressure. Other less-common side effects include chest pain or discomfort; difficult or labored breathing; dizziness; pounding or irregular heartbeat; pain or discomfort in the arms, jaw, back, or neck; and puffiness around the eyes, face, lips, or tongue (DailyMed, *Methylergonovine*, 2020).

Oxytocin is contraindicated in hypersensitivity, obstetric emergencies that negatively affect either the birthing parent or fetus, during fetal distress, when vaginal delivery is inadvisable or fetal positions/presentations are not favorable for delivery, and in uterine contraction pattern dysfunction.

The maternal side effects of oxytocin include nausea, vomiting, cardiac dysrhythmias, uterine hypertonicity, uterine rupture, postpartum hemorrhage, pelvic hematoma, water intoxication, and dilutional hyponatremia. Side effects for the fetus include bradycardia and other cardiac dysrhythmias, impaired fetal oxygenation, permanent brain or central nervous system (CNS) damage, and retinal hemorrhage.

Table 36.12 is a drug prototype table for oxytocics featuring oxytocin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Oxytocic **Mechanism of Action** Exerts a selective action on the smooth musculature of the uterus and stimulates rhythmic contractions of the uterus, increases the frequency of existing contractions, and raises the tone of the uterine musculature	**Drug Dosage** *Continuous infusion:* 1 mL (10 units/mL) combined with 1000 mL of an isotonic diluent such as lactated Ringer's solution. *Initial dose:* No more than 1–2 mU/minute; may be gradually increased in increments of no more than 1–2 mU/minute until normal labor contraction pattern established. *To control postpartum bleeding:* 10–40 units added to 1000 mL of a nonhydrating diluent. Rate adjusted as necessary to control uterine atony. 1 mL (10 units) of oxytocin intramuscularly after delivery of placenta.
Indications Initiation or improvement of uterine contraction **Therapeutic Effects** Induces labor and promotes contractions postpartum Stimulates lactation Facilitates delivery of fetus in some abortion situations	**Drug Interactions** Cyclopropane anesthesia (may modify oxytocin's cardiovascular effects) **Food Interactions** No significant interactions
Adverse Effects (Birthing Parent) Nausea Vomiting Cardiac dysrhythmias Uterine hypertonicity Uterine rupture Postpartum hemorrhage Pelvic hematoma Water intoxication Dilutional hyponatremia **Adverse Effects (Fetus)** Bradycardia and other cardiac dysrhythmias Impaired fetal oxygenation Permanent brain or central nervous system damage Retinal hemorrhage	**Contraindications** Hypersensitivity Obstetric emergencies that negatively affect either birthing parent or fetus Fetal positions/presentations that are not favorable for delivery Fetal distress When vaginal delivery is inadvisable Uterine contraction pattern dysfunction

TABLE 36.12 **Drug Prototype Table: Oxytocin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Tocolytics

Tocolytics are drugs used to delay contractions to prevent premature labor and the associated risks, including death of the infant. Magnesium sulfate ($MgSO_4$) is the drug used for this purpose. The indications for a tocolytic drug are premature labor after 20 weeks' gestation and generally prior to the 34th week. The purpose of using a tocolytic is to delay labor long enough (24 hours–7 days) to administer corticosteroids to the birthing parent. This allows for

fetal lung development to progress to a point where the fetus has enough surfactant to prevent respiratory distress after delivery.

$MgSO_4$ acts as a CNS and muscular depressant by preventing the peripheral neuromuscular transmission of acetylcholine. Also, $MgSO_4$ is a calcium antagonist, thus blocking calcium from entering cells and causing muscle contractions.

As a tocolytic agent, $MgSO_4$ use is controversial. Its primary use is controlling the seizures of preeclampsia or eclampsia in the birthing parent. It can possibly slow uterine contractions long enough to administer corticosteroids to the birthing parent, but current research does not support this belief. $MgSO_4$ is a drug that can cause sudden and severe adverse effects, and the client must be monitored closely. Any change in mental status such as decreased level of consciousness or confusion, sudden drop in blood pressure, loss of patellar reflex, depressed respirations, or hypermagnesemia should be treated immediately to prevent complete cardiovascular collapse and death. The treatment for magnesium toxicity is intravenous calcium gluconate or calcium chloride.

$MgSO_4$ can also be significantly detrimental to the fetus. It can cause hypocalcemia, skeletal demineralization, osteopenia, and bone and skeletal abnormalities if used more than 5–7 days during fetal development. The infusion during labor can lead to heart rate changes, hypotonia, respiratory depression, and possibly death.

Table 36.13 is a drug prototype table for tocolytics featuring magnesium sulfate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Tocolytic/antiseizure **Mechanism of Action** Blocks neuromuscular transmission Calcium antagonist	**Drug Dosage** Initial dose: 10–14 g. *Continuous infusion:* 4 g in 5% dextrose at a rate generally not to exceed 150 mg/minute, or 7.5 mL of a 2% concentration (or its equivalent) per minute. *Intramuscular:* Simultaneously administer 2 injections of 4–5 g (32.5–40.6 mEq) each.
Indications Maternal seizure activity Preterm labor **Therapeutic Effects** Prevention and control of seizures in preeclampsia and eclampsia Slows uterine contractions	**Drug Interactions** Aminoglycosides Amphotericin B Cyclosporine Diuretics Digitalis Cisplatin CNS depressants such as barbiturates, narcotics, or other hypnotics (or systemic anesthetics) **Food Interactions** Alcohol
Adverse Effects (Birthing Parent) Flushing Sweating Hypotension Depressed reflexes Flaccid paralysis Hypothermia Circulatory collapse Cardiac and central nervous system depression proceeding to respiratory paralysis Hypocalcemia with signs of tetany	**Contraindications** Hypersensitivity Toxemia of pregnancy during the 2 hours preceding delivery Myocardial damage Diabetic coma Heart block Hypermagnesemia Hypercalcemia Caution: Use extremely cautiously in myasthenia gravis and other muscular diseases and in clients with renal conditions

TABLE 36.13 **Drug Prototype Table: Magnesium Sulfate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Abortifacients

Abortifacients are medications used to evacuate the uterus via powerful contractions. These contractions empty the uterus of implanted **trophoblasts**, the cells that become the placenta, and prevent any fertilized egg from being implanted. Abortifacients are used during weeks 12–20 to terminate a pregnancy or to expel the fetus in cases of fetal demise. Carboprost and mifepristone are the drugs in this category.

The topic of abortion is highly controversial in the United States. The U.S. Supreme Court overturned the *Roe v. Wade* precedent in 2022. Thus, each U.S. state now writes and enacts its own legislation regarding abortion. In some states, health care professionals can be criminally charged for various actions related to abortions. Because nurses may be in situations that could involve some aspect of abortion, they should be cognizant of the abortion laws in the state where they practice. Each state's nurses' association and board of nursing, as well as the American Nurses Association, are resources nurses can contact for any questions or concerns about abortion laws. (See this American Nurses Association website on Sexual and Reproductive Health (https://openstax.org/r/nursingworld) for additional resources.)

Table 36.14 lists common abortifacients and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Carboprost (Hemabate)	Initial dose of 1 mL (250 mcg) deep intramuscular injection with tuberculin syringe. Subsequent doses of 250 mcg should be administered at 1½–3½ hour intervals depending on uterine response.
Mifepristone (Mifeprex, Korlym)	*Day 1:* One 200 mg tablet orally. *Day 2 or 3:* 200 mcg misoprostol tablets, total dose 800 mcg, buccal route. Minimum 24-hour interval between mifepristone and misoprostol doses.

TABLE 36.14 **Drug Emphasis Table: Abortifacients** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of abortifacients include abdominal cramping, heavy bleeding, headache, nausea, vomiting, diarrhea, backache, diaphoresis. Uterine perforation or rupture are also possible side effects.

Contraindications include drug allergy, active pelvic inflammatory disease, and acute cardiac, renal, hepatic, or pulmonary disease. These drugs should also not be used by lactating clients unless an alternative feeding method is possible. Caution should be used if a client has a history of asthma, hypertension, adrenal disease, vaginitis, or uterine scarring.

Table 36.15 is a drug prototype table for abortifacients featuring mifepristone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Abortifacient **Mechanism of Action** Empties the uterus of implanted trophoblasts, the cells that become the placenta, and prevents any fertilized egg from being implanted	**Dose** *Day 1:* One 200 mg tablet orally. *Day 2 or 3:* 200 mcg misoprostol tablets, total dose 800 mcg, buccal route. Minimum 24-hour interval between mifepristone and misoprostol doses.
Indications Medical termination of intrauterine pregnancy through 70 days gestation **Therapeutic Effects** Termination of pregnancy	**Drug Interactions** Rifampin Dexamethasone St. John's wort Phenobarbital Carbamazepine **Food Interactions** Grapefruit and grapefruit juice
Adverse Effects Abdominal cramping Heavy bleeding Headache Nausea Vomiting Diarrhea Backache Diaphoresis Uterine perforation or rupture	**Contraindications** Drug allergy Active pelvic inflammatory disease Acute cardiac, hepatic, or pulmonary disease Confirmed or suspected ectopic pregnancy or undiagnosed adnexal mass Chronic adrenal failure (risk of acute adrenal insufficiency) Concurrent long-term corticosteroid therapy (risk of acute adrenal insufficiency) History of allergy to mifepristone, misoprostol, or other prostaglandins Hemorrhagic disorders or concurrent anticoagulant therapy (risk of heavy bleeding) Termination of intrauterine pregnancy in clients with an IUD in place

TABLE 36.15 **Drug Prototype Table: Mifepristone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking uterine motility drugs:

- Assess client's medical and drug history as appropriate for the setting.
- Determine drug allergies.
- Assess client's labor and delivery status (active, complicated, patterns, cervical dilation, contractions, etc.)
- Assess client's mental and neurological status and vital signs, as well as fetal status, and monitor throughout procedure and as indicated.
- Initiate appropriate maternal and fetal monitoring equipment such as cardiac monitor and fetal heart rate monitor.
- Assess any contraindications/precautions for the specific medication to be used.
- Determine age of fetus (for abortifacients).
- Monitor laboratory values as ordered and indicated.
- Provide emotional support.
- Establish seizure precautions as needed.
- Initiate and maintain intravenous access.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLINICAL TIP

Administration of Mifepristone

- Inform the client that uterine bleeding and uterine cramping will occur
- Advise the client that serious and sometimes fatal infections and bleeding can occur very rarely.
- Mifepristone tablets, 200 mg, are only available through a restricted program called the Mifepristone REMS (Risk Evaluation and Mitigation Strategy) Program:
  - Clients must sign a Client Agreement Form.
  - Mifepristone tablets are only available by or under the supervision of certified prescribers or by certified pharmacies on prescriptions issued by certified prescribers.
- Misoprostol must be taken with mifepristone and within the specified time in order for a successful termination of pregnancy.

CLIENT TEACHING GUIDELINES

The client taking a uterine motility drug should:

- Understand the indications, side effects, and contraindications of the specific drug being used in their situation.
- Be able to give informed consent to the use of the drugs (if necessary).
- Report any serious side effects (prolonged severe cramping, heart palpitations, chest pain, difficulty breathing or shortness of breath, muscle weakness).
- If drug is used at home, take medication as prescribed.
- Contact the health care provider with any questions or concerns.
- Go to the nearest hospital emergency department for emergent situations (fever, severe abdominal pain, prolonged heavy bleeding, or syncope) or for abdominal pain or discomfort, general malaise, weakness, nausea, vomiting, or diarrhea occurring more than 24 hours after taking misoprostol.

The client taking a uterine motility drug *should not:*

- Stop taking or take a different dose of the medication than prescribed by their health care provider.
- Clients taking methylergonovine should avoid consuming grapefruit or grapefruit juice.
- Smoke or drink alcohol.
- Engage in sexual activity.
- Exercise or engage in strenuous activity.

FDA BLACK BOX WARNING

Mifepristone

Mifepristone can significantly increase the risk of death due to sepsis.

Drugs During Pregnancy and Lactation

Drug therapy must be approached cautiously during pregnancy, as some medications may have serious effects for the pregnant client or the fetus. Medications can be passed to the fetus through the placental membrane. Some medications are **teratogenic**, meaning they can cause serious birth defects, especially if given within the first trimester. The most critical period for fetal development is from conception to day 58–60 when major fetal organs form. Although some medications can pose risks of harm to the fetus, some maternal conditions such as pregnancy-induced hypertension or gestational diabetes may also cause harm. The situation must be viewed from a perspective of risks versus benefits to the birthing parent and fetus/infant. The emphasis for medications that treat a maternal condition is on choosing the safest drug from a class and monitoring the client more closely. In this way, the risks can be mitigated, even if not eliminated.

After delivery, special precautions are still needed for clients who are breastfeeding, as some medications can be transferred to the infant through breast milk. The National Library of Medicine (NLM) maintains the LactMed® database (https://openstax.org/r/ncbinlmnihgov) of drug information on relevant medications that clients who are breastfeeding may be exposed to (National Library of Medicine, n.d.). When assessing clients, nurses should determine if clients are breastfeeding and review the clients' medications for any potential concerns. Nurses should instruct clients to contact their health care provider first before taking any medication while breastfeeding to reduce the risk of adverse effects on the infant.

36.4 Bisphosphonates, Calcium Preparations, Vitamin D, and Estrogen Receptor Modulators

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 36.4.1 Identify the characteristics of bisphosphates, calcium, vitamin D, and estrogen receptor modulator drugs used to treat osteoporosis.
- 36.4.2 Explain the indications, actions, adverse reactions, and interactions of bisphosphates, calcium, vitamin D, and estrogen receptor modulator drugs used to treat osteoporosis.
- 36.4.3 Describe nursing implications of bisphosphates, calcium, vitamin D, and estrogen receptor modulator drugs used to treat osteoporosis.
- 36.4.4 Explain the client education related to bisphosphates, calcium, vitamin D, and estrogen receptor modulator drugs used to treat osteoporosis.

Bisphosphonates, calcium preparations, vitamin D, and estrogen receptor modulators may seem out of context in this chapter; however, they are included because of their effects on postmenopausal clients who no longer produce sufficient estrogen and are at increased risk of osteopenia and osteoporosis. **Osteopenia** is a condition in which bone mass is decreased, causing bones to become weaker. **Osteoporosis** is a condition in which bone mass has decreased to the point that bones become brittle and are much more likely to fracture (Fink, 2019; Zareef & Jackson, 2021; National Institutes of Health, 2022).

(See Thyroid and Parathyroid Disorder Drugs for more information regarding bisphosphonates, calcium preparations, and vitamin D.)

Bisphosphonates

Bisphosphonates are a category of drugs used to prevent and treat osteoporosis in postmenopausal clients. Vitamin D and calcium may be used as an adjunct with bisphosphonate therapy. Weight-bearing exercises, such as walking for 30 minutes several days a week, should be included as part of client education. Routine bone density testing should be scheduled to determine the effectiveness of the drug therapy (Ganesan et al., 2022).

Table 36.16 lists common bisphosphonates and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Alendronate (Fosamax)	10 mg orally once daily or 70 mg orally once weekly.
Ibandronate (Boniva)	*Oral:* 150 mg once monthly. *IV:* 3 mg every 3 months.
Risedronate (Actonel)	5 mg orally once daily, or 35 mg once weekly, or 150 mg once monthly.
Zoledronic acid (Reclast)	5 mg IV once every 12 months or 24 months for treatment of osteoporosis.

TABLE 36.16 Drug Emphasis Table: Bisphosphonates (sources: https://dailymed.nlm.nih.gov/dailymed/; Fink, 2019).

Adverse Effects and Contraindications

Adverse effects of bisphosphonates include decreased serum calcium and serum phosphate levels, arthralgia, myalgia, stomach pain, difficulty swallowing, heartburn, and irritation or pain of the esophagus. One major adverse effect from bisphosphonate therapy is osteonecrosis of the jaw (Madhumati & Gonegandla, 2020). The

bisphosphonate accumulates in the jaw at a higher rate than in other bones and causes increased new bone formation. As a result, the older bone lacks sufficient blood supply and begins to die or become necrosed. This complication occurs more often in clients with cancer and in those who have invasive dental procedures. Thus, invasive dental procedures should not be performed while a client is receiving bisphosphonates.

Contraindications to bisphosphonates include any esophageal abnormality that prevents adequate and timely emptying of the stomach. Additionally, bisphosphonates should not be used if the client is unable to sit up or stand for at least 30 minutes after taking the medication, to reduce the risk of esophageal irritation. Severe renal insufficiency is another instance where bisphosphonates should not be used.

Table 36.17 is a drug prototype table for bisphosphonates featuring alendronate. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Bisphosphonates **Mechanism of Action** Inhibits normal and abnormal bone resorption	**Drug Dosage** 10 mg orally once daily or 70 mg orally once weekly (may vary depending on indication).
Indications Prevention and treatment of osteoporosis in postmenopausal clients For the treatment of osteoporosis in males, Paget's disease, and glucocorticoid-induced osteoporosis **Therapeutic Effects** Increases bone density	**Drug Interactions** Calcium Antacids Aspirin Nonsteroidal anti-inflammatory drugs (NSAIDs) **Food Interactions** No significant interactions unless food or beverages (except water) are taken within 30 minutes of drug Avoid orange juice for at least 2 hours after taking
Adverse Effects Decreased serum calcium and serum phosphate levels Arthralgia Myalgia Stomach pain Difficulty swallowing Heartburn Irritation or pain of the esophagus Osteonecrosis of the jaw	**Contraindications** Esophageal abnormalities that prevent adequate and timely emptying of the stomach Inability of client to sit up or stand for at least 30 minutes after taking the medication (to reduce risk of esophageal irritation) Severe renal insufficiency

TABLE 36.17 **Drug Prototype Table: Alendronate** (source: https://dailymed.nlm.nih.gov/dailymed/)

Calcium Preparations

Calcium, the most abundant mineral in the body, is necessary for bone development and bone maintenance. In fact, about 98% of the body's calcium is stored in the bones. Calcium from food and supplements is absorbed by both active transport and passive diffusion across the intestinal mucosa. Vitamin D is essential for calcium absorption and for maintaining adequate calcium levels. Estrogen is also important for maintaining bone health; thus, during menopause when females produce less estrogen, they have a considerable risk of developing osteopenia and osteoporosis (National Institutes of Health, 2022).

Food sources of calcium include dairy, salmon, dark green vegetables (broccoli, kale, spinach), and other foods with high levels of oxalic acid such as sweet potatoes, rhubarb, and beans. Calcium supplements vary widely as to their source and the amount of calcium contained in the tablets (National Institutes of Health, 2022).

Calcium supplements include calcium acetate, calcium citrate, calcium gluconate, and calcium chloride. Calcium supplements used to treat osteoporosis and osteopenia are administered orally; dosages depend on the specific type of calcium supplement being prescribed and the reason for its use. Calcium carbonate and calcium citrate are

the two most common forms of calcium used in supplements. Calcium has varying rates of absorption depending on the specific supplement, an individual's level of stomach acid, and the fat content in a meal eaten when a calcium supplement is taken. The greater the fat content, the less calcium is absorbed. Calcium gluconate and calcium chloride are administered intravenously and used for serious and life-threatening acute hypocalcemia, hyperkalemia, and certain cardiac emergencies. See Fluids and Electrolytes, Vitamins, Minerals, and Alternative Therapies for more information about calcium and Vitamin D.

Adverse Effects and Contraindications

Adverse effects of calcium supplements are usually GI related and include abdominal pain, gas, bloating, constipation, and nausea. Hypercalcemia can lead to poor muscle tone, renal insufficiency, weight loss, fatigue, polyuria, and heart arrhythmias.

Contraindications and precautions are necessary depending on the client's chronic diseases and other medications being taken. Clients with heart disease and renal disease may need closer monitoring of calcium levels. Calcium supplements generally decrease stomach acid necessary for the metabolism and absorption of other medications. Levothyroxine is one example; it should be taken at least 30 minutes prior to or 2 hours after calcium. So a complete medication history is important in planning calcium supplementation.

Vitamin D

Along with calcium supplements, vitamin D should be taken either as a separate supplement or included in the calcium supplement. The best source of vitamin D is sunlight. The appropriate amount of time for sun exposure is determined by the skin type based on Fitzpatrick's skin typing, which ranges from I (fair skin that burns easily) to VI (skin that is always tan) (National Institutes of Health, 2022; Sakamoto, 2019; Zareef & Jackson, 2021). The use of sunscreen during sun exposure is controversial as far as the effect on vitamin D; however, the client should take care to avoid sunburn (AIM at Melanoma Foundation, n.d.).

Other sources of vitamin D include fatty fish (such as trout, salmon, tuna, and mackerel) and fish liver oils and fortified foods such as milk and cereals (National Institutes of Health, 2022).

Estrogen Receptor Modulators

Estrogen receptor modulators (ERMs) are not hormones. They are estrogen receptor site agonists or antagonists. ERMs possess some of the positive effects of estrogen and have fewer adverse effects. Raloxifene and toremifene are the drugs discussed in this section.

Raloxifene

Raloxifene is used to prevent and treat postmenopausal osteoporosis by increasing bone density. Contraindications include allergy, pregnancy, and lactation. Caution should be used for clients with a history of deep vein thrombosis and/or smoking because of the risk of clot development. Adverse effects are like those of estrogen and can include skin rash and edema. Raloxifene dosage is 60 mg daily orally.

Table 36.18 is a drug prototype table for estrogen receptor modulators featuring raloxifene. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Estrogen receptor modulator **Mechanism of Action** Binds to estrogen receptors with either activation of estrogenic pathways (agonism) or blockade of estrogenic pathways (antagonism)	**Drug Dosage** 60 mg orally once daily. Supplemental calcium and/or vitamin D should be added to the diet if daily intake is inadequate.
Indications Prevention and treatment of osteoporosis in postmenopausal clients **Therapeutic Effects** Increases bone density	**Drug Interactions** Cholestyramine Warfarin Systemic estrogens Use with caution with certain other highly protein-bound drugs such as diazepam, diazoxide, and lidocaine **Food Interactions** No significant interactions
Adverse Effects Venous thromboembolism Skin rash Edema Hot flashes Leg cramps Nausea Arthralgia Rhinitis	**Contraindications** Allergy Pregnancy and lactation History of deep vein thrombosis, pulmonary embolism, or retinal vein thrombosis and/or smoking because of the risk of clot development

TABLE 36.18 **Drug Prototype Table: Raloxifene** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Raloxifene

Raloxifene may cause increased risk of venous thromboembolism and death from stroke in clients with a history of venous thrombosis, documented coronary heart disease, or at increased risk for major coronary events.

Toremifene

Toremifene is used to treat clients who have estrogen receptor–positive advanced breast cancer. Toremifene works by binding to estrogen receptors, which prevents cancer cells from developing. Contraindications include allergy to the drug, pregnancy and lactation, and hypercalcemia. Caution must be used in prescribing toremifene to clients with renal or hepatic dysfunction or bone marrow suppression. Adverse effects are like menopausal symptoms, which were discussed in Review of the Female Reproductive System.

Table 36.19 is a drug prototype table for estrogen receptor modulators featuring toremifene. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Estrogen receptor modulator **Mechanism of Action** Binds to estrogen receptors, which prevents cancer cells from developing	**Drug Dosage** 60 mg orally once daily. Supplemental calcium and/or vitamin D should be added to the diet if daily intake is inadequate.
Indications Treatment for female clients who have estrogen receptor–positive advanced breast cancer **Therapeutic Effects** Prevents cancer cells from growing and spreading	**Drug Interactions** Thiazide diuretics Drugs that prolong QT interval (quinidine, procainamide, disopyramide, amiodarone, sotalol, ibutilide, dofetilide) Strong CYP3A4 enzyme inducers, such as dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, phenobarbital, St. John's wort **Food Interactions** Grapefruit or grapefruit juice
Adverse Effects Venous thromboembolism Hot flashes Nausea and vomiting Fatigue Depression Lethargy Anorexia Arthritis Pulmonary embolism Myocardial infarction	**Contraindications** Allergy Pregnancy and lactation Prolonged QT interval Renal or hepatic impairment

TABLE 36.19 **Drug Prototype Table: Toremifene** (source: https://dailymed.nlm.nih.gov/dailymed/)

FDA BLACK BOX WARNING

Toremifene

Toremifene may cause QT prolongation, which could result in a type of ventricular tachycardia called torsade de pointes, which may result in syncope, seizure, and/or death.

Nursing Implications

The nurse should do the following for clients who are taking bisphosphonates, calcium preparations, vitamin D, or estrogen receptor modulators:

- Perform a physical assessment and determine the reason for the specific drug therapy.
- Assess past medical history and family history for osteoporosis, hypocalcemia, and vitamin D deficiency.
- Assess the client's ability to understand and follow medication regimen.
- Determine pregnancy and lactation status.
- Assess smoking history and use of alcohol.
- Obtain necessary diagnostic and laboratory testing, such as bone density, calcium and vitamin D levels, and electrocardiogram.
- Assess diet and exercise patterns.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a bisphosphonate, calcium, vitamin D, or an estrogen receptor modulator should:

- Understand the medication's purpose, side effects, contraindications, precautions, and any signs and symptoms to report that require immediate attention.
- Know how to manage the side effects of the specific drug therapy.
- Know the medication dosage and route and be able to self-administer correctly (e.g., drink at least 6–8 ounces of water with bisphosphonate and remain standing or sitting upright for 30 minutes after taking the medication).
- Maintain weight-bearing exercise of 30 minutes 3–5 times weekly to increase bone strength.
- Include foods high in calcium in diet: leafy green vegetables, salmon, dairy, sweet potatoes, rhubarb, and beans.
- Understand drug, food, or herbal interactions with the specific medication.
- Verbalize the importance of follow-up appointments and diagnostic testing to manage the medication regimen.

The client taking a bisphosphonate, calcium, vitamin D, or an estrogen receptor modulator *should not:*

- Take bisphosphonates at the same time as other medications or supplements.
- Take calcium supplements with a high-fat meal.

36.5 Review of the Male Reproductive System

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 36.5.1 Describe the structure and function of the male reproductive system.
- 36.5.2 Discuss common conditions that affect the male reproductive system.

Structure and Function of the Male Reproductive System

The male reproductive system (also referred to as the testicular reproductive system) is made up of internal and external organs (see Figure 36.5). The external organs include the scrotum, testes, epididymis, and penis. The internal organs are the vas deferens, prostate gland, ejaculatory ducts, seminal vesicles, bulbourethral (Cowper's) glands, and urethra (Betts et al., 2023; Netter, 2022).

The scrotum is a loose, sac-like cavity that holds the testicles and provides a controlled temperature for them since temperature within the scrotum is lower than in the body itself. The testicles produce sperm, which fertilize an egg from a female. The epididymis carries the formed sperm into the vas deferens, which then empties the sperm into the ejaculatory duct in the body of the prostate gland. Two seminal vesicles, one on each side of the prostate, also empty into the ejaculatory duct. From the ejaculatory duct, the sperm enter the urethra. The bulbourethral (Cowper's) glands secrete mucus into the urethra, and both the mucus and sperm are carried outside the body through the urethra. The penis contains sensory nerves that respond to sexual stimulation and cause the penis to become enlarged and elongated. Contractions of the penis allow the sperm, along with other secretions, to empty outside the body. The primary target would be the uterus where the sperm fertilizes the egg, creating the embryo that implants into the uterus and further develops into the fetus (Betts et al., 2023; Netter, 2022). (Refer to Section 36.1.)

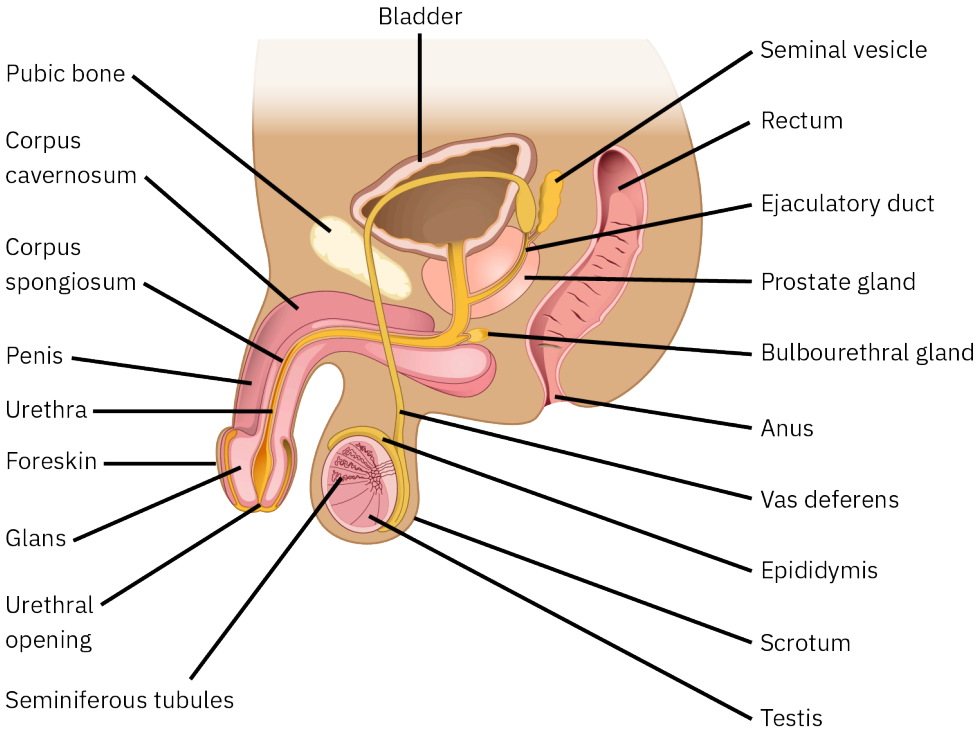


FIGURE 36.5 The internal and external male reproductive system is sometimes also referred to as the testicular reproductive system. (credit: modification of work from *Biology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Hormones

Some of the same hormones that are produced in individuals assigned female at birth are also produced in those assigned males at birth, and those include GnRH and the gonadotropins, LH and FSH. As discussed in Review of the Female Reproductive System, GnRH is produced in the hypothalamus. When GnRH is secreted, it acts on the anterior pituitary to secrete FSH and LH, which regulate sex steroid production from the gonads. In males, the gonads are the testes (ovaries in females) which produce testosterone (also considered an androgen). Testicular hormones are responsible for the development of male sex organs and secondary sex characteristics, including hair distribution (pubic area, axillae, facial, and chest), voice deepening, heavier bone structure, increased hematocrit, and fat distribution. Additionally, testosterone can self-limit its own secretion through the negative feedback loop. When levels of testosterone are high, feedback to the hypothalamus inhibits the secretion of GnRH. Negative feedback to the anterior pituitary renders it less responsive to GnRH stimuli (Casteel & Singh, 2023; Nassar, 2023).

Andropause

Andropause occurs with aging and represents a time of decreased production of testosterone, atrophy of interstitial cells, and lessened sexual activity. Andropause is comparable to female menopause. The decrease of testosterone can produce depression, fat redistribution, and decreased libido. Not all male clients experience andropause.

LINK TO LEARNING

Male Menopause

Access multimedia content (https://openstax.org/books/pharmacology/pages/36-5-review-of-the-male-reproductive-system)
What is “male menopause”? An expert breaks down everything clients need to know about andropause in this Daily Mail video.

36.6 Androgens, Antiandrogens, and Anabolic Steroids

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 36.6.1 Identify the characteristics of androgen, antiandrogen, and anabolic steroid drugs used to treat reproductive disorders.
- 36.6.2 Explain the indications, actions, adverse reactions, and interactions of androgen, antiandrogen, and anabolic steroid drugs used to treat reproductive disorders.
- 36.6.3 Describe nursing implications of androgen, antiandrogen, and anabolic steroid drugs used to treat reproductive disorders.
- 36.6.4 Explain the client education related to androgen, antiandrogen, and anabolic steroid drugs used to treat reproductive disorders.

Androgens, antiandrogens, and anabolic steroids drugs are natural and synthetic forms of testicular hormones. They are used to treat hypogonadism, delayed male puberty, and some types of female breast cancer. They can also be used off-label for stimulation of appetite and to increase muscle mass in malignancy and acquired immunodeficiency syndrome (AIDS) (Ganesan et al., 2023).

Androgens

Androgens are sex hormones. Testosterone is the primary androgen and is produced in the testes. The other androgens are produced in the adrenal glands. Testosterone is responsible for the growth and development of male sex organs and the secondary sex characteristics such as voice deepening, hair distribution, and redistribution of muscle and fat. It also contributes to bone growth, red blood cell production, decreased excretion of calcium in the urine, and the retention of sodium, potassium, and phosphorous.

Hypogonadism is the condition where the testes are undeveloped and fail to produce androgen, sperm, or both. Males with hypogonadism do not experience puberty. **Delayed puberty** is when the sex characteristics do not develop at the expected time in puberty. Clients experiencing either condition may need exogenous hormone therapy to develop sex organs and secondary sex characteristics.

The prototype androgen is testosterone. It comes in oral, parenteral, topical, implantable, and buccal forms. Dosage and frequency vary depending on the form of the drug and the individual need of the client. Table 36.20 lists common androgens and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Testosterone (Depo-testosterone, Androderm)	*Male hypogonadism/delayed puberty:* *Depo-testosterone:* 50–400 mg intramuscularly every 2–4 weeks. *Androderm:* 4 mg/day transdermal patch (adjusted per serum testosterone concentration).
Fluoxymesterone (Halotestin)	*Male hypogonadism/delayed puberty:* 5–20 mg daily orally. *Breast cancer treatment in postmenopausal females:* 10–40 mg/day orally.
Methyltestosterone (Methitest)	*Hypogonadism, delayed puberty in males:* 10–50 mg daily orally. *Breast cancer treatment in postmenopausal females:* 50–200 mg/day orally.

TABLE 36.20 **Drug Emphasis Table: Androgens** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

The adverse effects of testosterone for males include gynecomastia, prolonged penile erections, and decreased ejaculatory volume. For females taking testosterone for advanced breast cancer, side effects are generally related to masculinization—voice deepening, clitoral enlargement, and hirsutism. Menstrual irregularities and amenorrhea may develop in premenopausal clients.

Androgens are contraindicated in hypersensitivity to the drug, male breast and prostate cancer, and serious cardiac, hepatic, or renal disease. Additionally, testosterone must be used cautiously in prepubescent clients because of the possibility of early bone maturation and early closure of the epiphyseal growth plates. This condition can lead to stunted growth. When young clients are on testosterone therapy, they need radiographs every 6 months to monitor bone maturation.

Clients with preexisting gynecomastia may have a worsening of the condition. Older clients may have an increased risk of benign prostatic hyperplasia (BPH) and prostate cancer. Clients with BPH may develop urethral obstruction. Testosterone is contraindicated for pregnant clients because it can cause masculinization of the female fetus, and the risks of the drug outweigh the potential benefits for pregnant clients. See Urinary and Bladder Disorder Drugs for more about BPH and its treatment.

Table 36.21 is a drug prototype table for androgens featuring testosterone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Androgen **Mechanism of Action** Binds to and activates androgen receptors	**Drug Dosage** *Male hypogonadism/delayed puberty:* *Depo-testosterone:* 50–400 mg intramuscularly every 2–4 weeks. *Androderm:* 4 mg/day transdermal patch (adjusted per serum testosterone concentration).
Indications Replacement therapy in conditions associated with symptoms of deficiency or absence of endogenous testosterone **Therapeutic Effects** Development of male sex characteristics	**Drug Interactions** Oral anticoagulants May decrease blood glucose levels in clients with diabetes, so hyperglycemic drug doses may need to be decreased **Food Interactions** No significant interactions
Adverse Effects Hypercalcemia in immobilized clients Gynecomastia Excessive frequency and duration of penile erections Hirsutism Male pattern baldness Seborrhea Acne Nausea Cholestatic jaundice Alterations in liver function tests Venous thromboembolism Increased or decreased libido Headache Anxiety Depression	**Contraindications** Known hypersensitivity to the drug Male breast cancer Prostate cancer Pregnancy Serious cardiac, hepatic, or renal disease Caution: Benign prostatic hyperplasia

TABLE 36.21 **Drug Prototype Table: Testosterone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Antiandrogens

Antiandrogens are medications that compete with testosterone for androgen-receptor binding sites; in other words, they work against androgens and testosterone. Antiandrogens either prevent these hormones from binding to proteins in the target cells or decrease the amount of a hormone produced. Antiandrogens are used to treat advanced prostate cancer. Bicalutamide is the primary medication used. It should be taken in combination with a gonadotropin-releasing hormone analog to treat metastatic prostate cancer.

Antiandrogens are frequently used in combination with gonadotropin-releasing hormone analogs to treat advanced prostate cancer (Freedland & Abrahamsson, 2021). These two groups of medications have different mechanisms of action, but both decrease testosterone to nonexistent levels comparable to surgical castration.

Adverse Effects and Contraindications

Contraindications for the use of antiandrogens are allergy to the drug or its components and liver dysfunction or elevated liver enzymes. The adverse effects of antiandrogens include gynecomastia, breast pain, hot flashes,

decreased libido, impotence, diarrhea, anemia, and abnormal liver function. Liver failure can occur.

Table 36.22 is a drug prototype table for antiandrogens featuring bicalutamide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antiandrogen **Mechanism of Action** Inhibits the action of androgens by binding to cytosol androgen receptors in the target tissue	**Drug Dosage** 50 mg orally daily (along with a luteinizing hormone–releasing hormone [LHRH] analog).
Indications Treatment of stage D2 metastatic carcinoma of the prostate **Therapeutic Effects** Stops the growth and spread of cancer cells	**Drug Interactions** Coumadin **Food Interactions** No significant interactions
Adverse Effects Pain (general) Back pain Asthenia Pelvic pain Infection Abdominal pain Chest pain Headache Flu syndrome Hot flashes Nausea Leg cramps Hypercholesteremia Elevated liver enzymes Gynecomastia	**Contraindications** Known hypersensitivity to the drug or its components Use in female clients Pregnancy

TABLE 36.22 **Drug Prototype Table: Bicalutamide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Anabolic Steroids

Anabolic steroids are analogues of testosterone developed for use in tissue building in conditions such as illness or surgery that have caused significant wasting of tissue, weight loss, and depletion of red blood cells. Oxandrolone is the primary anabolic steroid. It is indicated for weight gain and cancer treatment. The dosage for oxandrolone is 2.5 mg–20 mg, two to four times daily, administered orally.

Both androgens and anabolic steroids stimulate protein synthesis in skeletal muscle and thus increase the buildup of cellular tissue. They also stimulate increased production of red blood cells. For those reasons, androgens and anabolic steroids are used in clients who are debilitated by chronic illnesses (e.g., cancer, HIV, anemias), trauma, long-term steroid use, or surgery in order to increase muscle mass, gain weight, repair tissue, and increase red blood cell count (Ganesan et al., 2023).

Adverse Effects and Contraindications

In general, anabolic steroids can cause electrolyte imbalances, liver damage, insomnia, weight gain, acne, depression, anxiety, aggression, increased cholesterol and low-density lipoprotein levels, hypertension, and changes in the structure of the left ventricle of the heart (DailyMed, *Oxandrolone tablet*, 2022).

The adverse effects in prepubertal clients include phallic enlargement, hirsutism, and increased skin pigmentation. In postpubertal clients, side effects can include decreased testicular function and testicular atrophy, gynecomastia, priapism, baldness, and changes in libido. Prostate problems, especially in older clients, may also be a side effect of

these drugs. Female clients may experience hirsutism, voice deepening, clitoral enlargement, baldness, reduced breast volume, and menstrual irregularities (DailyMed, *Oxandrolone tablet*, 2022).

These medications are contraindicated in allergy to the drug, pregnancy and lactation, liver or coronary heart disease, nephrosis, hypercalcemia, and breast or prostate cancer in males (DailyMed, *Oxandrolone tablet,* 2022).

All anabolic steroids are DEA Schedule III drugs; however, anabolic steroids and testosterone have been misused by many athletes, both professional and amateur, for the purposes of bodybuilding and enhancing physical performance in sports (Chegeni et al., 2021; Ganesan et al., 2023; Schneider et al., 2020). These drugs are not approved to be used for bodybuilding or enhancing physical performance and, thus, are not prescribed by health care professionals for those purposes, nor are they permitted by athletic competition boards.

Table 36.23 is a drug prototype table for anabolic steroids featuring oxandrolone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Anabolic steroid **Mechanism of Action** Inhibits the action of androgens by binding to cytosol androgen receptors in the target tissue	**Drug Dosage** 2.5–20 mg orally given in 2–4 divided doses.
Indications Adjunctive therapy to offset the protein catabolism associated with prolonged administration of corticosteroids **Therapeutic Effects** Relief of the bone pain frequently accompanying osteoporosis Weight gain and muscle building	**Drug Interactions** Coumadin Oral hypoglycemic medications Adrenal steroids or adrenocorticotropic hormone (ACTH) **Food Interactions** No significant interactions
Adverse Effects Cholestatic jaundice Habituation Excitation Insomnia Depression Changes in libido Edema Retention of serum electrolytes (sodium chloride, potassium, phosphate, calcium) Decreased glucose tolerance Increased creatinine excretion Increased serum creatinine phosphokinase (CPK) Inhibition of gonadotropin secretion Hepatic necrosis and death (rare) *In Prepubertal Males:* Phallic enlargement and increased frequency or persistence of erections *In Postpubertal Males:* Inhibition of testicular function Testicular atrophy Oligospermia Impotence Chronic priapism Epididymitis Bladder irritability Gynecomastia *In Females:* Clitoral enlargement Menstrual irregularities Deepening of the voice Hirsutism and male pattern baldness Masculinization of the fetus	**Contraindications** Known hypersensitivity to the drug or its components Use in female clients Pregnancy Known or suspected prostate or male breast cancer Female breast cancer with hypercalcemia Nephrosis Hypercalcemia Caution: Clients with moderate to severe chronic obstructive pulmonary disease (COPD) and who are unresponsive to bronchodilators should be monitored closely for COPD exacerbation and fluid retention

TABLE 36.23 **Drug Prototype Table: Oxandrolone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking androgens, antiandrogens, anabolic steroids, or GnRH analogues:

- Determine the reason for use of androgens, antiandrogens, anabolic steroids, or GnRH analogues.
- Assess understanding of indication for specific drug therapy and ability to comprehend instructions.
- Perform gender- and age-appropriate physical assessment, including height, weight, and blood pressure.
- Assess past medical history and family history for cardiovascular disease (heart attack, stroke, hypertension), pregnancy/lactation status, breast or prostate cancer, gynecomastia, and BPH.
- Obtain medication list including OTC and herbal remedies.
- Assess smoking history and use of alcohol.
- Obtain pertinent diagnostic testing such as long bone radiographs and laboratory studies for liver and renal function, complete blood count, serum chemistries, and lipids, and monitor as necessary.
- Assess ability to administer drug at home and follow medication regimen.
- Monitor for any misuse of drug therapy.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an androgen, antiandrogen, anabolic steroid, or GnRH analogue should:

- Understand the medication's purpose, side effects, contraindications, and precautions.
- Understand the medication dosage and route and be able to self-administer correctly (oral, patch, injections).
- Monitor any signs and symptoms of adverse effects and report those that require immediate attention.
- Monitor and record pertinent observations such as weight, height, and blood pressure as instructed.
- Monitor and report emotional and/or behavioral changes to health care provider.
- Know how to manage the side effects of various hormonal medications.
- Understand drug, food, and/or herbal interactions that could be harmful. See drug prototype tables for specific drugs.
- Verbalize the importance of follow-up appointments to manage the medication regimen and to observe for adverse effects.

The client taking an androgen, antiandrogen, anabolic steroid, or GnRH analogue *should not:*

- Alter the dosage or abruptly discontinue these medications.
- Smoke or consume alcohol.

FDA BLACK BOX WARNING

Oxandrolone

Oxandrolone can cause serious liver problems, including hepatitis and tumors, and serum lipid changes that could cause coronary heart disease.

Oxandrolone may accelerate bone maturation without producing compensatory gain in linear growth, a condition called premature closure of epiphyses in children. This adverse effect results in compromised adult height.

36.7 Phosphodiesterase 5 Inhibitors

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 36.7.1 Identify the characteristics of phosphodiesterase 5 inhibitor drugs used to treat erectile dysfunction.
- 36.7.2 Explain the indications, actions, adverse reactions, and interactions of phosphodiesterase 5 inhibitor drugs used to treat erectile dysfunction.
- 36.7.3 Describe nursing implications of phosphodiesterase 5 inhibitor drugs used to treat erectile dysfunction.
- 36.7.4 Explain the client education related to phosphodiesterase 5 inhibitor drugs used to treat erectile dysfunction.

Phosphodiesterase 5 (PDE5) inhibitors are used to treat erectile dysfunction. PDE5 is an enzyme located within the walls of blood vessels that impacts blood flow. PDE5 inhibitors prevent the PDE5 enzyme from functioning, which results in the relaxation of the blood vessels and increased blood flow. PDE5 inhibitors work in cases when blood flow to the corpus cavernosum is inadequate, such as in aging or due to vascular or neurological problems. However, these medications cannot be used for every cause of erectile dysfunction, and they do have serious side effects if taken incorrectly, such as taking more than one dose in 24 hours or taking with nitroglycerin. Sildenafil, tadalafil, avanafil, and vardenafil are the common PDE inhibitors. (Use of PDE5 inhibitors for treating benign prostatic hyperplasia is discussed in Urinary and Bladder Disorder Drugs).

Table 36.24 lists common PDE5 inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Sildenafil (Viagra)	50 mg orally, as needed, approximately 60 minutes before sexual activity. Dose range: 25–100 mg. Maximum of 1 dose/day.
Tadalafil (Cialis)	10 mg orally, as needed, approximately 60 minutes before sexual activity. Dose range: 5–20 mg. Maximum of 1 dose/day.
Avanafil (Stendra)	100 mg orally, as needed, as early as approximately 15 minutes before sexual activity. Dose range: 50–200 mg. Maximum of 1 dose/day.
Vardenafil (Levitra)	10 mg orally, as needed, approximately 60 minutes before sexual activity. Dose range: 5–20 mg. Maximum of 1 dose/day.

TABLE 36.24 **Drug Emphasis Table: Phosphodiesterase 5 Inhibitors** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Contraindications for PDE5 inhibitors include the concomitant use of nitrates or alpha-adrenergic blockers, medications often prescribed for cardiovascular problems. The drug interaction can cause life-threatening hypotension and death. Another contraindication is any obstructive condition or anatomical deformation of the penis (DailyMed, *Viagra*, 2019; Dhaliwal & Gupta, 2023).

Table 36.25 is a drug prototype table for PDE5 inhibitors featuring sildenafil. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Phosphodiesterase 5 inhibitor **Mechanism of Action** Smooth muscle relaxation and inflow of blood to the corpus cavernosum	**Drug Dosage** 50 mg orally, as needed, approximately 1 hour before sexual activity. Dose range: 25–100 mg. Maximum of 1 dose/day.
Indications Male erectile dysfunction **Therapeutic Effects** Enhanced penile erection	**Drug Interactions** Nitrates (all forms) Alpha blockers Strong CYP3A4 inhibitors **Food Interactions** No significant interactions
Adverse Effects Headaches Flushing Symptoms resembling those of the common cold Stomach upset Muscle and back pain Dizziness, lightheadedness Nausea Abnormal vision Nasal congestion	**Contraindications** Known hypersensitivity to the drug or its components Caution: History of heart attack, heart failure, angina, severe arrhythmia, or stroke in the last 6 months Hypotension or hypertension (resting BP <90/50 mm Hg or BP >170/110 mm Hg) Hepatic impairment Severe renal impairment Anatomical deformation of the penis

TABLE 36.25 **Drug Prototype Table: Sildenafil** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking phosphodiesterase 5 inhibitors:

- Assess understanding of indication for specific drug therapy and ability to comprehend instructions.
- Perform physical assessment as appropriate and obtain any diagnostic testing necessary.
- Obtain list of current medications and any OTC or herbal remedies the client uses, especially regarding nitrates and alpha blockers.
- Assess past medical history and family history for cardiovascular disease (heart attack, stroke, hypertension, serious arrhythmias), prostate cancer, BPH, and liver or renal disease.
- Assess smoking history and use of alcohol.
- Assess ability to administer drug at home and follow medication regimen.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a phosphodiesterase 5 inhibitor should:

- Understand the medication's purpose, side effects, contraindications, and precautions.
- Monitor any signs and symptoms of adverse effects and report those that require immediate attention (e.g., vision or hearing loss, priapism).
- Know how to manage the side effects of the specific drug therapy.
- Understand drug, food, and/or herbal interactions that could be harmful.
- Verbalize the importance of follow-up appointments to manage the medication regimen and to observe for adverse effects.

The client taking a phosphodiesterase 5 inhibitor *should not:*

- Take nitrates and alpha blockers within 48 hours of taking PDE5 inhibitors.
- Take these medications after a high-fat meal.

FDA BLACK BOX WARNING

Phosphodiesterase 5 (PDE5) Inhibitors

PDE5 inhibitors can cause:

- Severe hypotension and death when used within 48 hours of any form of nitrate medication
- Prolonged erection greater than 4 hours and priapism (painful erections greater than 6 hours in duration)
- Sudden loss of vision in one or both eyes (may be a sign of nonarteritic anterior ischemic optic neuropathy)
- Sudden decrease in or loss of hearing

36.8 Alpha Blockers and 5-Alpha-Reductase Inhibitors

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 36.8.1 Identify the characteristics of alpha blockers and 5-alpha-reductase inhibitor drugs used to treat benign prostatic hyperplasia (BPH).
- 36.8.2 Explain the indications, actions, adverse reactions, and interactions of alpha blockers and 5-alpha-reductase inhibitor drugs used to treat benign prostatic hyperplasia (BPH).
- 36.8.3 Describe nursing implications of alpha blockers and 5-alpha-reductase inhibitor drugs used to treat benign prostatic hyperplasia (BPH).
- 36.8.4 Explain the client education related to alpha blockers and 5-alpha-reductase inhibitor drugs used to treat benign prostatic hyperplasia (BPH).

Benign Prostatic Hyperplasia

Benign prostatic hyperplasia (BPH) is the nonmalignant enlargement of the prostate gland. This condition usually begins in mid-life and increases in prevalence as male individuals age. Studies have reported that about 8% of males in the fourth decade of life have BPH. That number increases significantly to about 50% in the sixth decade of life and 80% in the ninth decade of life (GBD 2019 Benign Prostatic Hyperplasia Collaborators, 2022; Ng & Barahdi, 2022). Two primary classes of medications used to treat BPH are **alpha blockers** and **5-alpha-reductase inhibitors**.

BPH is also associated with complications such as urinary tract infection, acute urinary retention, urolithiasis, and acute renal failure as well as impacting other aspects of life, such as sleep quality, mood, social and sexual well-being, and safety related to increased falls (GBD 2019 Benign Prostatic Hyperplasia Collaborators, 2022).

Alpha Blockers

Alpha blockers are indicated to treat BPH. They work by relaxing the smooth muscle of the bladder neck and prostate to allow for an easier flow of urine. Alpha blockers include alfuzosin, doxazosin, tamsulosin, silodosin, and terazosin. Clients with smaller prostates often experience results more quickly.

Alpha blockers should be taken daily at the same meal, either breakfast or dinner (evening meal).

Table 36.26 lists common alpha blockers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Tamsulosin (Flomax)	0.4 mg orally once daily. May be increased to 0.8 mg once daily after 2–4 weeks if needed.
Doxazosin (Cardura)	1 mg given once daily either in the morning or evening. May be increased at 1- to 2-week intervals to 2 mg, 4 mg, and 8 mg daily (maximum dose).

TABLE 36.26 **Drug Emphasis Table: Alpha Blockers** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Alfuzosin (Uroxatral)	10 mg extended-release tablet orally once daily.
Silodosin (Rapaflo)	8 mg orally once daily.
Terazosin (Prostera)	1 mg orally once daily at bedtime. May increase to 2 mg, 5 mg, and 7.5 mg gradually once daily.

TABLE 36.26 **Drug Emphasis Table: Alpha Blockers** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects might include dizziness and hypotension, especially when combined with other drugs that lower blood pressure. Retrograde ejaculation may occur, a harmless condition in which semen goes back into the bladder instead of out the tip of the penis. Other adverse effects include priapism, somnolence, dry mouth, dyspnea, fatigue, palpitations, headache, upper respiratory infections, abdominal pain, dyspepsia, constipation, nausea, and impotence.

Since clients with BPH could have coexisting erectile dysfunction, they may also take PDE5 inhibitors. Concomitant use of alpha blockers and PDE5 inhibitors can cause a severe drop in blood pressure. Additionally, signs and symptoms of prostate cancer and BPH are similar. Thus, ruling out cancer as the underlying issue is a priority before initiating alpha blockers.

Table 36.27 is a drug prototype table for alpha blockers featuring tamsulosin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Alpha blocker **Mechanism of Action** Relaxes the smooth muscle of the bladder neck and prostate	**Drug Dosage** 0.4 mg orally once daily. May be increased to 0.8 mg once daily after 2–4 weeks if needed.
Indications Treatment of the signs and symptoms of benign prostatic hyperplasia **Therapeutic Effects** Allows easier flow of urine through the ureter	**Drug Interactions** Ketoconazole and similar drugs Erythromycin Cimetidine PDE5 inhibitors **Food Interactions** Grapefruit and grapefruit juice
Adverse Effects Dizziness, vertigo Retrograde ejaculation Postural hypotension Priapism	**Contraindications** Hypersensitivity

TABLE 36.27 **Drug Prototype Table: Tamsulosin** (source: https://dailymed.nlm.nih.gov/dailymed/)

5-Alpha-Reductase Inhibitors

The 5-alpha-reductase inhibitors such as finasteride and dutasteride block conversion of testosterone to dihydrotestosterone, resulting in shrinkage of the prostate gland. Improvement is not seen until the client has been on the medication for several weeks. Maximum results should occur about 6 months after the start of treatment. The prostate-specific antigen (PSA) can be decreased about 50%, and the prostate volume may be reduced by as much as 25% (Ng & Baradhi, 2022; Salisbury & Tadi, 2023).

Indications for 5-alpha-reductase inhibitors are BPH and male pattern baldness, but this section focuses only on

BPH. Table 36.28 lists common 5-alpha-reductase inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Finasteride (Proscar, Propecia)	5 mg orally once daily.
Dutasteride (Avodart)	0.5 mg orally once daily.

TABLE 36.28 **Drug Emphasis Table: 5-Alpha-Reductase Inhibitors** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects related to 5-alpha-reductase inhibitors include erectile dysfunction, decreased ejaculatory volume, decreased libido, gynecomastia, orthostatic hypotension, dizziness, and weakness. Dutasteride may be combined with an alpha blocker to enhance the treatment of BPH. If so, the client has a greater chance of experiencing orthostatic hypotension, dizziness, and weakness.

Table 36.29 is a drug prototype table for 5-alpha-reductase inhibitors featuring finasteride. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class 5 alpha-reductase inhibitor **Mechanism of Action** Shrinks the size of the prostate gland	**Drug Dosage** 5 mg orally once daily.
Indications BPH Male pattern baldness **Therapeutic Effects** Improves urine flow in males	**Drug Interactions** Drugs that cause hypotension and dizziness may increase the risk of these side effects **Food Interactions** No significant interactions
Adverse Effects Hypotension Dizziness Increase in high-grade prostate cancer Breast changes including neoplasm Erectile dysfunction Libido, ejaculation, and orgasm disorders Male infertility	**Contraindications** Hypersensitivity Pregnancy

TABLE 36.29 **Drug Prototype Table: Finasteride** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients using alpha blockers or 5-alpha reductase inhibitors:

- Conduct history and physical to determine any underlying condition, such as prostate cancer, that should be treated first. Also determine other medical conditions that may be impacting urological health (diabetes, cardiovascular, obesity, etc.).
- Obtain medication history, noting any medications that may interact with alpha blockers or alpha reductase inhibitors (drugs that may cause hypotension or dizziness).
- Obtain necessary laboratory and diagnostic testing.
- Assess smoking and alcohol use.
- Assess balance and alertness because hypotension and dizziness are side effects of both alpha blockers and alpha reductase inhibitors. Somnolence is a side effect of alpha blockers.
- Provide emotional support and resources for client.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client

teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an alpha blocker or a 5-alpha-reductase inhibitor should:

- Understand the medication's purpose, side effects, contraindications, and precautions. Take alpha blocker medications ½ hour following the same meal each day (either breakfast or dinner/evening meal).
- Understand the risks to females, especially pregnant females, of handling crushed or broken tablets (5-alpha-reductase inhibitors).
- Monitor any signs and symptoms of adverse effects and report them to the health care provider.
- Know how to manage the side effects of specific 5-alpha-reductase inhibitor therapy, especially related to safety (risk of falls).
- Know how to manage the side effects of specific alpha blocker therapy (dizziness, priapism, hypotension).
- Verbalize the importance of follow-up appointments to manage the medication regimen and to observe for adverse effects.
- Understand drug, food, and/or herbal interactions that could be harmful.
- Use caution when driving, operating machinery, or performing other tasks requiring alertness when taking alpha blockers.

The client taking an alpha blocker or a 5-alpha-reductase inhibitor *should not:*

- Change position quickly when taking alpha blockers to minimize the risk of postural hypotension, especially when taking other medications that lower blood pressure.
- Not allow females of childbearing age to handle 5-alpha-reductase inhibitors, especially if the tablets are crushed or broken.

Chapter Summary

This chapter discussed the male and female reproductive systems, hormones involved in their development, and various conditions that can occur throughout a client's lifespan. Major ovarian hormones include estrogen, progestin, FSH, LS, and GnRH. Major testicular hormones include FSH, LS, GnRH, testosterone, and androgens. Hormonal drugs are used to replace low levels of natural hormones, treat some types of cancers, prevent pregnancy, minimize symptoms of menopause, and treat debilitated clients who need tissue building and increased red blood cells. Reproductive hormones are produced naturally by the body and have complex effects. Synthetic hormones have been developed for administration when natural hormone replacement is not possible. Nurses must be aware of the intricate ways in which hormones are interrelated and affect health and illness overall.

Medications used in special situations such as infertility, pregnancy, labor, and postlabor were discussed. These include drugs that can either delay (tocolytics) or stimulate (oxytocics) uterine contractions during labor and delivery, the use of abortifacients, and fertility drugs. There are also special considerations when using drugs during pregnancy and lactation. Drugs used for menopause include hormone replacement therapy and medications that treat conditions that can develop during menopause, such as osteopenia and osteoporosis. Bisphosphonates, calcium, vitamin D, and estrogen receptor modulators (ERMs) are used to treat those conditions. Male-specific conditions treated with medications include hypogonadism, delayed puberty, erectile dysfunction, and BPH. Some testicular hormones (testosterone) and anabolic steroids are used to treat clients with debilitative conditions such as chronic illness or who may have had long-term steroid use.

Key Terms

5-alpha-reductase inhibitors medication used to treat BPH; works by shrinking the prostate gland

abortifacients medications that cause complete evacuation of the contents of the uterus

alpha blockers medication used to treat BPH; works by relaxing the smooth muscle of the prostate and bladder neck

anabolic steroids a category of medications, analogues to testosterone, used to enhance tissue building and stimulate production of red blood cells

andropause time of decreased production of testosterone, atrophy of interstitial cells, and lessened sexual activity; comparable to female menopause

antiandrogens medications that compete with testosterone for androgen-receptor binding sites and work against androgens and testosterone

combined oral contraceptives (COCs) contraceptive drugs that contain both estrogen and progestin in varying dosages; the three categories are *monophasic* (contain a fixed ratio of estrogen and progestin), *biphasic* (contain a fixed dose of estrogen with a varying dose of progestin), and *triphasic* (contain low doses of both estrogen and progestin with a varying dose of estrogen)

contraceptives medications and devices that prevent a female from becoming pregnant

delayed puberty condition when the male sex characteristics do not develop at the expected time in puberty

estradiol hormone used primarily for relief of menopause symptoms; used for hormone replacement therapy

estrogen primary hormone released by the ovaries; initiates the development of female genitalia and breast tissue

estrogen receptor modulators (ERMs) nonhormone drugs that stimulate or block estrogen receptor sites; used to treat osteoporosis in postmenopause

first-day start method a method of initiating a contraceptive when the client starts the contraceptive on day 1 of the menstrual cycle and continues as directed

follicle-stimulating hormone (FSH) gonadal hormone secreted by the anterior pituitary in response to GnRH; stimulates development of ovarian follicles and release of mature ovum from mature follicles; prepares the body for and supports pregnancy until delivery

gonadotropin-releasing hormone (GnRH) a hormone produced in and released by the hypothalamus that acts as the central regulator; responsible for regulating the start of puberty, the onset of the menstrual cycle, the development of sex characteristics, and ovulation

hormone replacement therapy (HRT) the use of hormones postmenopause to decrease symptoms and complications of menopause

hypogonadism condition in which testes are undeveloped and the development of sex organs

and secondary sex characteristics is delayed or absent

implanted contraceptive devices devices containing a hormone that are place under the skin of the inner upper arm for the purpose of contraception

intrauterine devices (IUD) devices containing either a hormone or copper, designed to be placed within the uterus for the purpose of contraception

lactation the secretion of breast milk by the mammary glands

luteinizing hormone (LH) gonadal hormone secreted by the anterior pituitary in response to GnRH; stimulates development of ovarian follicles and release of mature ovum from mature follicles; prepares the body for and supports pregnancy until delivery

menarche initial menstrual cycle of a female

menopause the cessation of monthly cycles for one year

menstrual cycle cycle of hormone secretion, follicular and ova development, and preparation and shedding of endometrial lining that occurs monthly in females

osteopenia the condition in which bone is losing density

osteoporosis the condition when bone loss is significant and bone has become porous and brittle

oxytocics medications that stimulate the uterus to contract

perimenopause the time when a menstrual cycle undergoes changes preparing for the end of the ability to ovulate and to become pregnant

phosphodiesterase 5 (PDE5) inhibitors a group of medications developed to aid in penile erection for the purpose of sexual intercourse

pregnancy the period of time a fetus grows inside the uterus

progesterone primary hormone released by the ovaries; performs many of the same functions as estrogen does to promote maturation of sex organs, prepare the body for pregnancy, and maintain a healthy uterine environment for development of the fetus

progestin-only contraceptives contraceptive drugs that do not have estrogen; they only contain progestin

quick start method a method of initiating oral contraception drugs where the client takes the first dose of the medication on the day of the visit rather than waiting until after a monthly period begins

sexually transmitted infections (STIs) infections involving internal and external sex organs that are transmitted by sexual intercourse or intimate contact with sex organs; may be viral, bacterial, or fungal

Sunday start method a method of initiating oral contraceptive drugs where the client takes the first dose of medication on the first Sunday after a menstrual period starts

teratogenic any substance taken by the birthing parent that can cause serious birth defects in a fetus

tocolytics medications that delay uterine contractions by relaxing the uterine muscle

trophoblasts the outer layer of cells of an embryo, which become the placenta

Review Questions

1. A young female client is discussing the various methods of contraception with the nurse. Which factor is most important for the nurse to consider in counseling the client?
   a. Client reports a history of migraine headaches.
   b. Client has an irregular menstrual cycle.
   c. The client's sexual history.
   d. The cost of the contraceptive method.

2. A client in labor is receiving an oxytocin infusion. Which signs and symptoms are a priority for the nurse to assess further?
   a. Maternal heart rate of 102 beats/minute and blood pressure of 146/90 mm Hg
   b. Sudden onset of confusion and muscle cramps
   c. Client-reported headache of 4 out of 10 on the pain scale
   d. Urine output of 100 mL/hour

3. A 68-year-old male client comes to the emergency department with chest pain. Before administering the ordered sublingual nitroglycerin, which question is most important for the nurse to ask the client?
   a. "How long have you had the chest pain?"
   b. "Do you have a history of cardiac problems?"

c. "When did you last eat or drink anything?"
d. "Do you take any medications for erectile dysfunction?"

4. An 11-year-old client is undergoing hormone therapy with testosterone for hypogonadism. Which assessment is most important for the nurse to monitor?
a. Results of radiographic images of the long bones every 6 months
b. Serum hemoglobin and hematocrit monthly
c. Serum electrolytes weekly
d. Blood pressure and electrocardiogram weekly

5. The nurse is caring for a client in labor who will be receiving an $MgSO_4$ infusion for eclampsia. Which provider's order is most important to implement?
a. Continuous cardiac monitoring
b. Hourly urine output
c. Nothing by mouth (NPO)
d. Oxygen saturation monitoring

6. A male high school student who plays on the football team has been referred to the school nurse. He reports feeling anxious and irritable, and his stomach bothers him most of the time. He tells the nurse, "I never had acne problems, but now it's terrible. And my hair is falling out." What question by the nurse would be most appropriate?
a. "Do you have a family history of depression or anxiety?"
b. "Are you eating a lot of greasy or spicy foods?"
c. "Are you taking anything to help you build up your muscle strength?"
d. "How many hours of sleep are you getting each night?"

7. A postmenopausal female is at high risk for developing osteoporosis. Her provider has prescribed alendronate. Which statement by the client indicates a need for further teaching by the nurse?
a. "I need to sit or stand for 30 minutes after taking the medication."
b. "I should drink a full glass of water with the medication."
c. "Walking 30 minutes a day can help prevent my bones from becoming weak."
d. "I can go ahead and have a tooth that is bothering me pulled."

8. A 45-year-old client with prostate cancer is undergoing treatment with bicalutamide. Which problem is a priority for the nurse to address?
a. Risk for injury: impaired liver function
b. Disturbed body image
c. Chronic pain
d. Risk for imbalanced nutrition

9. A postmenopausal client is taking a bisphosphonate medication. Which diagnostic testing for this client does the nurse expect to be a priority?
a. Electrocardiogram and stress testing
b. Bone density
c. Venous ultrasound
d. Upper endoscopy

10. A client with a chronic illness is taking an anabolic steroid. Which condition indicates the drug is having a therapeutic effect?
a. Increased hemoglobin
b. Hirsutism
c. Worsening acne
d. Alopecia

CHAPTER 37
Transgender and Nonbinary Drugs

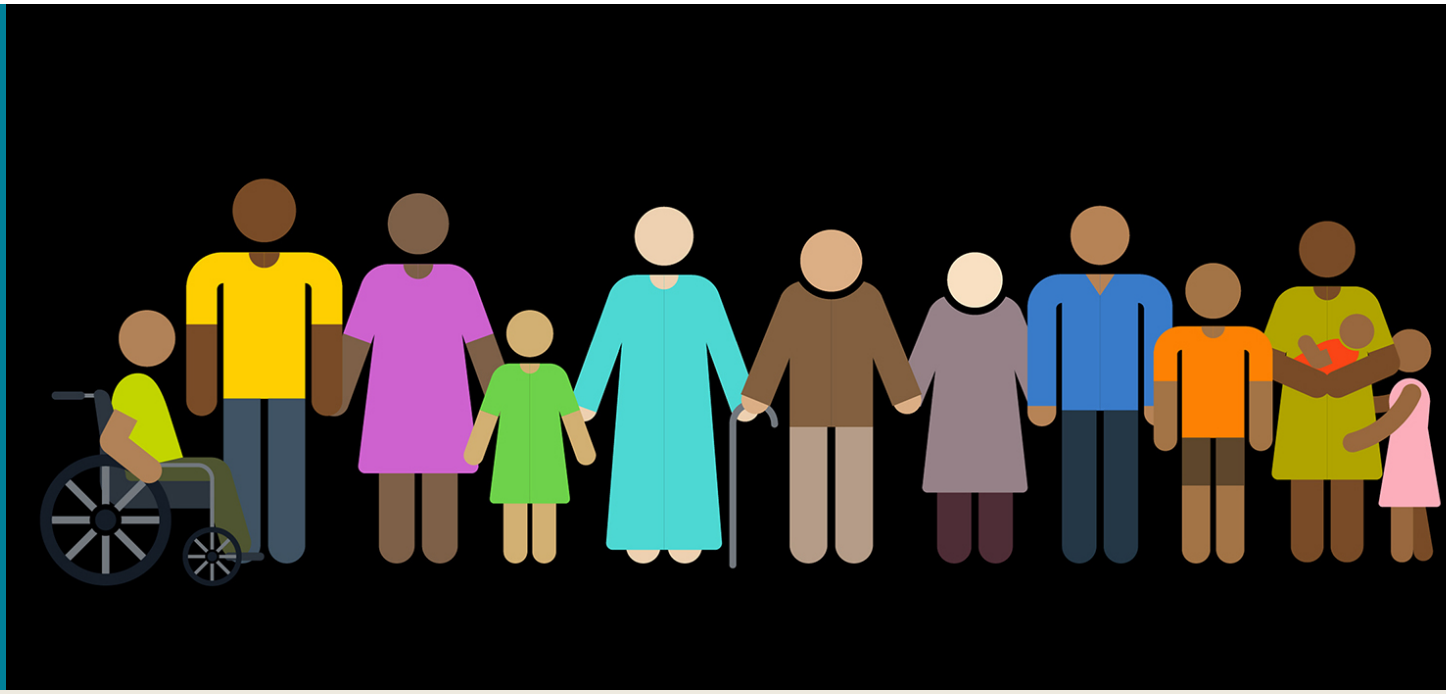


FIGURE 37.1 Supporting reproductive health involves caring for clients in a variety of life stages and with different gender expressions. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION Transgender and nonbinary health care encompasses many aspects. This chapter begins by listing and defining some of the preferred terms used to refer to transgender and nonbinary individuals. An important issue for nurses and other health care professionals to remember is that each transgender or nonbinary individual may have their own preferred words. Therefore, an important first step in caring for these clients is finding out what those words are.

This chapter then introduces the medications used to enhance or modify sexual characteristics including nursing implications and client education. Some of the medications in this chapter are also covered in Reproductive Health Drugs, but this chapter focuses on their use for adjusting sexual characteristics.

37.1 Overview of Transgender and Nonbinary Health

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 37.1.1 Differentiate among terms related to gender identity.
- 37.1.2 Identify clinical manifestations related to gender dysphoria.

Often, **gender nonconforming** individuals do not experience health care access in an accepting, nonthreatening, affirming, and supportive climate. In fact, some individuals have been so traumatized by their experiences that they forgo important medical care and preventive services. Numerous articles (Brooker & Loshak, 2020; Dickerson, 2022; Gonzales & Henning-Smith, 2017; Kinney & Cosgrove, 2022; Kirkland et al., 2021; Milionis et al., 2022; Sirufo et al., 2022) discuss barriers and challenges to adequate and sensitive health care for gender nonconforming

individuals. The full range of barriers and challenges are too numerous to recount in this chapter; however, all health care professionals, whether they work exclusively within the transgender and nonbinary population or in general health care settings, should be knowledgeable about the various needs of the transgender and nonbinary population.

Additionally, a self-assessment concerning personal bias and beliefs about transgender and nonbinary individuals is necessary for any health care professional who interacts with these particular clients. Understanding one's own beliefs and feelings, and acknowledging any bias or prejudice, is the first step in a nurse's acceptance of transgender and nonbinary individuals' decisions. Being respectful and professional is important for creating and maintaining a trusting relationship with transgender and nonbinary clients (Barredo, 2020).

Terms Related to Gender Identity

Gender identity describes a person's deeply held beliefs about which, if any, gender they identify with—man, woman, gender fluid, or nonbinary. A person's gender identity is not always the same as the sex assigned at birth and is not always related to an individual's sexual organs or sex characteristics. Instead, it refers to how an individual sees themselves and presents themselves to others as male and/or female.

The following terms are used to discuss gender-related topics. Individual clients will have their own terms to describe themselves, and the nurse must clarify those with each client. A client may find some terms to be offensive, and their use would compromise trust in the nurse–client relationship (Annie E. Casey Foundation, 2023; Barredo, 2020; Centers for Disease Control and Prevention, 2023; International Society for Sexual Medicine, n.d.; National Center for Transgender Equality, 2016; Rafferty et al., 2018; T'Sjoen et al., 2019).

- **Gender dysphoria** a deep sense of unease, anxiety, or discomfort that may occur in people whose gender does not align with their sex assigned at birth.
- **Gender expression** refers to ways in which a person outwardly expresses their gender identity. Gender expression includes behavior, clothing, body characteristics, and/or voice. Gender expression may or may not conform to what is considered socially acceptable male and female behaviors and characteristics.
- **Gender fluid** refers to a person who does not identify with a single fixed gender or has an unfixed gender identity.
- **Nonbinary** is used to describe individuals whose gender identity does not fit into the man–woman dichotomy and who do not identify with one gender over another. The term may be used to include individuals who are gender fluid and/or transgender.
- **Transgender** is a broad term used by individuals whose sex assigned at birth does not match their gender identity. Some transgender individuals are assigned male at birth but identify as a woman; others are assigned female at birth but identify as a man. Some transgender individuals do not identify strongly as a man or a woman, or they may identify as a combination of both genders. Some transgender individuals choose to have medical treatment to physically transition into the gender with which they identify; others choose not to undergo treatment. The male-to-female (MTF) and female-to-male (FTM) abbreviations are used in this chapter to refer to the procedure of transitioning.
- The term **transsexual** is an older term that may be interchangeable with the term *transgender*; however, transsexual has different meanings depending on the individual's preference, the cultural context, societal norms, and the historical meaning of the word. In addition, transsexual can be used by some to identify individuals who have undergone medical treatment and surgery to make their bodies physically match the gender with which they identify.
- **Cisgender** describes individuals whose sex assigned at birth and gender identity are congruent. A cisgender person assigned male at birth identifies as a man, and a cisgender person assigned female at birth identifies as a woman.

Clinical Manifestations of Gender Dysphoria

Gender dysphoria is a medical diagnosis that describes the condition of an individual who is experiencing social and mental distress because of gender identity issues. The feelings may range from unease to severe distress and can impair the individual's ability to function in society. Going to school, work, and other social events can be associated with fear and anxiety about harassment or mistreatment (Klein, 2023; Matsuda, 2022; National Center for Transgender Equality, 2016; Selby, 2022). The individual feels that their sex assigned at birth is incongruent with

their gender identity. These individuals are often adolescents or young adults who have faced a great deal of socially negative experiences because they do not identify with the sex that was assigned to them at birth. Zaliznyak et al. (2020) collected data from more than 200 transgender individuals and found that gender dysphoria tends to start very early in life. Among their study participants, the earliest memories of gender dysphoria generally began around 4 1/2 years of age, with the majority of participants experiencing gender dysphoria memories by age 7.

Gender dysphoria does not occur in every transgender individual, nor is every person who experiences gender dysphoria transgender (National Center for Transgender Equality, 2016). For those who do experience gender dysphoria, typical manifestations include depression, anger, anxiety, body aversion, posttraumatic stress disorder, hopelessness, violence, self-harm, and suicide. Some individuals with gender dysphoria may dress differently, change their name to match their perceived gender, and make other outward changes that are congruent with their gender identity (Klein, 2023; Matsuda, 2022; National Center for Transgender Equality, 2016; Selby, 2022).

Supporting Intersex People

Intersex is a general term used to describe people whose sex traits, reproductive anatomy, hormones, or chromosomes are different from the usual two ways human bodies develop. Some intersex traits are recognized at birth, while others are not recognizable until puberty or later in life. Intersex people and transgender people are not the same (and they are not interchangeable terms); many transgender people have no intersex traits, and many intersex people do not consider themselves transgender. Furthermore, most recent literature refers to the atypical conditions themselves as "differences of sex development," (DSD); nurses may find relevant guidance and evidence with that terminology, even though many intersex people do not use it to refer to themselves and some reject the terminology (Sandberg, 2022; Davis, 2013).

Most in the nursing, medical, and intersex community reject unnecessary surgeries intended to make a baby conform to a specific gender assignment (Behrens, 2020). If a physical trait or medical condition prohibits a baby from urinating or performing another bodily function (which is very rare), surgery may be needed. In other cases, intersex people may require hormonal therapies similar to those described below. Treatment of intersex clients, especially adolescents and adults, can be complex: Diagnoses, decisions, and therapies may have implications regarding the client's gender identity, gender role behavior, and sexual functioning, as well as physical and psychological outcomes (Sandberg, 2022; Warne, 2005).

Hormonal Therapy Guidelines for Transgender and Nonbinary Clients

Drug therapy of any kind is affected by several factors, including gender at birth, transgender status, weight, and overall health. Renal and liver cytochrome expression, renal or liver disease, age, and gastric pH also affect pharmacokinetics and pharmacodynamics. Webb et al. (2020) explored the literature regarding drug dosing for transgender individuals. In some cases, the dosing was comparable; for example, a transgender male's pharmacokinetics and pharmacodynamics were like those of a cisgender male, and drug dosing could be the same. However, appropriate dosing also depended on the length of time an individual had been on hormonal therapy. Thus, the nurse must ensure that any transgender client has been properly assessed for these factors and communicate this information to the health care provider, pharmacist, and other health care professionals as needed.

37.2 Feminizing Hormonal Therapy

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 37.2.1 Identify the characteristics of feminizing hormonal drugs used for transgender and nonbinary therapy.
- 37.2.2 Explain the indications, actions, adverse reactions, and interactions of feminizing hormonal drugs used for transgender and nonbinary therapy.
- 37.2.3 Describe nursing implications of feminizing hormonal drugs used for transgender and nonbinary therapy.
- 37.2.4 Explain the client education related to feminizing hormonal drugs used for transgender and nonbinary therapy.

The hormones used for female reproductive health, which are covered in Reproductive Health Drugs, are also discussed in this chapter; complete information for the drugs can be found there. Discussion in this chapter focuses on use of the medications for developing female secondary sex characteristics in individuals who were assigned male at birth and choose to undergo male-to-female (MTF) transition. These sex characteristics include fat redistribution around the hips, skin softening and decreased oiliness, growth of breast tissue, decreased muscle mass and strength, loss of facial hair, decreased libido and ejaculation volume, and decreased testicle size (Figure 37.2). The adverse effects of female hormone therapy are related to cardiovascular conditions such as myocardial infarction, stroke, and thromboembolic events. However, studies of transgender individuals are still limited in number, and more research is needed to explore the effects of female hormones on male clients (Deutsch, 2016; Hembree et al., 2017; Ramsay & Safer, 2023; Unger, 2016). Further transition would include surgery to remove the testes, as well as other feminizing surgical procedures (Mount Sinai, n.d.-b).

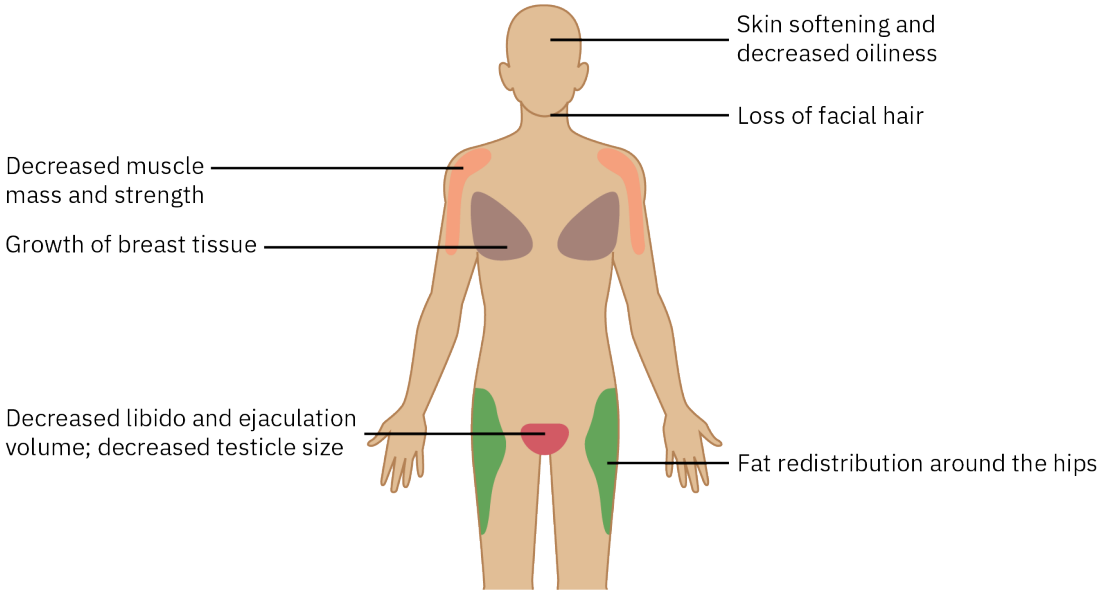


FIGURE 37.2 Drugs used for male-to-female transition affect many areas of the body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Spironolactone

Spironolactone is a nonspecific aldosterone blocker. Its primary use is as a potassium-sparing diuretic to manage hypertension. However, its action of blocking male sex hormone receptors, the androgen receptors, decreases the production of testosterone, the male hormone responsible for secondary sex characteristics (DailyMed *Spironolactone,* 2023; Deutsch, 2016; Hembree et al., 2017; Mayo Clinic, 2021a; Ramsay & Safer, 2023; Unger, 2016). Spironolactone is used for 4–8 weeks alone, and then estrogen is usually added. Spironolactone can cause impotence and **gynecomastia** (breast tissue enlargement) in males, a desired effect for males transitioning to females.

Adverse Effects and Contraindications

Contraindications include allergy to the drug, hyperkalemia, renal disease, and anuria (absent urine production and output). The primary adverse effect is hyperkalemia, which could be life-threatening and must be monitored closely. Hyperkalemia may manifest as lethargy, confusion, ataxia, muscle cramps, cardiac dysrhythmias (irregular heart rhythms), or gastrointestinal symptoms (DailyMed, *Spironolactone,* 2023; Unger, 2016).

Table 37.1 is a drug prototype table for spironolactone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Potassium-sparing diuretic Antiandrogen **Mechanism of Action** Blocks male sex hormone (androgen) receptors, resulting in decreased production of testosterone	**Drug Dosage** 100–200 mg/day orally; may be increased to 400 mg/day.
Indications Initial male-to-female transitioning hormonal treatment **Therapeutic Effects** Reverses/inhibits development of secondary male sex characteristics	**Drug Interactions** Angiotensin-converting enzyme (ACE) inhibitors Angiotensin receptor blockers Nonsteroidal anti-inflammatory drugs (NSAIDs) **Food Interactions** Salt substitutes containing potassium
Adverse Effects Hyperkalemia, with possible life-threatening cardiac rhythm disturbances and renal issues Abdominal pain Diarrhea Nausea and vomiting Chest pain Heart palpitations Muscle weakness Numbness in extremities	**Contraindications** Allergy or hypersensitivity to drug Renal disease Anuria Hyperkalemia Caution: ACE inhibitors Angiotensin receptor blocker medications

TABLE 37.1 **Drug Prototype Table: Spironolactone** (sources: https://dailymed.nlm.nih.gov/dailymed/; Deutsch, 2016; Hembree et al., 2017)

SAFETY ALERT

Spironolactone

Spironolactone may cause hyperkalemia because it is a potassium-sparing medication. The nurse should monitor the client's potassium levels and cardiac and renal function. Potassium may be found in intravenous fluids, salt substitutes, and some fruits and vegetables (including oranges, bananas, raisins and other dried fruits, and dark green and yellow vegetables).

Estrogen

The purpose of estrogen is to continue the development of secondary female sex characteristics. Estrogen works through a negative feedback loop to suppress gonadotropin secretion from the pituitary gland and results in reduced androgen production. Usually, estrogen alone will not achieve sufficient androgen control. Thus, antiandrogenic therapy, in the form of spironolactone, may need to be added to the client's medication regimen. Although this may seem contrary to the information regarding spironolactone—that is, starting spironolactone first and then adding estrogen—both regimens are acceptable. The specific medication regimen depends on the individual's needs (Deutsch, 2016; Hembree et al., 2017; Mayo Clinic, 2021a; Ramsay & Safer, 2023; Unger, 2016).

Clients will notice the onset of these characteristics: smaller testicles; fewer erections and a decrease in ejaculation; decreased libido; decreased male pattern baldness; breast development; softer, less oily skin; less muscle mass; and more body fat. These changes will usually begin 1–6 months after treatment starts. The full effect will take 2–3 years (Deutsch, 2016; Hembree et al., 2017; Mayo Clinic, 2021a; Ramsay & Safer, 2023; T'Sjoen et al., 2019; Unger, 2016).

Estradiol is the most potent form of estrogen and is naturally produced in the body. Estradiol is extremely beneficial prior to menopause and for use as postmenopausal hormone replacement therapy. It provides significant protection against cardiovascular disease and osteoporosis. It has been shown to work well in MTF transgender therapy also.

Estradiol can be administered orally, parenterally, and transdermally.

Table 37.2 lists common estrogen-based feminizing hormones and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Conjugated estrogens	2–6 mg/day orally.
17-beta-estradiol	2–4 mg /day orally.
Estradiol valerate	5–30 mg every 2 weeks intramuscularly.
Estradiol cypionate	2–5 mg/week intramuscularly.
Estradiol patch	0.1–0.4 mg twice weekly transdermally.

TABLE 37.2 Drug Emphasis Table: Estrogen-Based Feminizing Hormones (sources: Coleman et al., 2022; Deutsch, 2016)

Adverse Effects and Contraindications

A major contraindication for estrogen is a personal or family history of blood clots in the leg (deep vein thromboses) or lungs (pulmonary emboli). Estrogen should be used cautiously in clients who smoke, have obesity, or have hypertension (Mayo Clinic, 2021a; T'Sjoen et al., 2019; Unger, 2016).

Adverse effects of estrogen can include major cardiovascular problems (cardiac disease, elevated cholesterol, stroke, and hypertension), elevated prolactin levels, nipple discharge, and infertility (Mayo Clinic, 2021a; Milionis et al., 2022; T'Sjoen et al., 2019; Unger, 2016).

Table 37.3 is a drug prototype table for estrogen-based feminizing hormones featuring 17-beta-estradiol in the context of MTF transgender treatment. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Estrogen (hormone) **Mechanism of Action** Decreases testosterone production	**Drug Dosage** 2–4 mg/day orally (may vary depending on specific type of estrogen).
Indications Aids in MTF transition **Therapeutic Effects** Development of female sex characteristics: Increased breast size Weight gain and fat redistribution Softer, less oily skin Decreased facial hair Decreased muscle mass Decreased libido Decreased testicle size	**Drug Interactions** Ketoconazole Barbiturates Carbamazepine Phenytoin Penicillins Tetracyclines Rifampin St. John's wort False unicorn root Red clover Wild yam **Food Interactions** Grapefruit and grapefruit juice
Adverse Effects Blood clots (deep vein thromboses, pulmonary emboli) Increased triglycerides Stroke Myocardial infarction Hypertension Increased serum potassium Increased serum prolactin Nipple discharge Weight gain Infertility Type 2 diabetes Increased risk of hormone receptor–positive breast cancer	**Contraindications** Estrogen-sensitive cancer (prostate) Active or history of thrombophlebitis or thromboembolic problems Cardiovascular disease Smoking Hypersensitivity

TABLE 37.3 **Drug Prototype Table: 17-Beta-Estradiol** (sources: https://dailymed.nlm.nih.gov/dailymed/; Deutsch, 2016; T'Sjoen et al., 2019)

Progesterone

Progesterone is a hormone that is classified as a progestin and aids in the development of secondary female sexual characteristics. Progestins are metabolized by the liver and excreted in urine. Contraindications, precautions, and adverse events are similar to those for estrogen. (See Reproductive Health Drugs for more information about progesterone).

Progesterone can cause fluid retention and may adversely affect conditions that are worsened by fluid retention, including cardiovascular and renal diseases, asthma, and migraine headaches (DailyMed, *Medroxyprogesterone,* 2020). Clients undergoing MTF transition sometimes request progesterone to enhance breast enlargement. However, because there is no evidence that this is effective and because this treatment involves risks, progesterone therapy is not routinely used in transgender treatment (Hembree et al., 2017; T'Sjoen et al., 2019).

Table 37.4 is a drug prototype table for progesterone in the context of MTF transition treatment. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications. Most information regarding the use of progesterone in MTF transgender treatment is inconclusive because few studies have been conducted in this context (Deutsch, 2016; Hembree et al., 2017; Milionis et al., 2022; Ramsay & Safer, 2023; T'Sjoen et al., 2019).

Drug Class Progestin (female hormone) **Mechanism of Action** Antiandrogenic effect through central blockade of gonadotropins	**Drug Dosage** Dosages vary in the literature.
Indications Aids in MTF transition **Therapeutic Effects** (Based on anecdotal information from clients and providers) Improved breast and/or areolar development Improved mood Increased libido	**Drug Interactions** No significant interactions **Food Interactions** Grapefruit and grapefruit juice (inconclusive)
Adverse Effects Information is inconclusive.	**Contraindications** History of thrombotic events Cardiac, renal, or liver disease

TABLE 37.4 **Drug Prototype Table: Progesterone** (sources: https://dailymed.nlm.nih.gov/dailymed/; Deutsch, 2016)

FDA BLACK BOX WARNING

Estrogen Plus Progestin Therapy

The Women's Health Initiative (https://openstax.org/r/whi) studies demonstrated an increased risk of invasive breast cancer in clients treated with estrogen plus progestin therapy.

Gonadotropin-Releasing Hormone Analogs

The action of gonadotropin-releasing hormone (GnRH) analogs decreases the amount of testosterone produced, which lessens the development of male secondary sex characteristics. GnRH analogs have been used for transitioning transgender adults. They may allow the client to reduce the dose of estrogen and eliminate spironolactone from the treatment regimen. However, GnRH analogs tend to be more expensive than spironolactone and may not be covered by medical insurance. Additionally, GnRH analogs require repeated injections or multiple daily nasal sprays. For these reasons, GnRH analogs may not be the best choice for some clients (Deutsch, 2016; Hembree et al., 2017; Hruz, 2020).

One of the primary benefits of GnRH analog therapy is that once therapy is discontinued, the sex characteristics of the sex assigned at birth return. Therefore, a client who decides not to pursue transgender treatment will not have permanent changes to their body (Hembree et al., 2017; Hruz, 2020).

On the other hand, few studies have been completed regarding the use of GnRH analogs. Thus, some of the long-term effects, adverse effects, exact dosing, and best administration method have not been determined. Adverse effects that appear to be related to GnRH analog therapy include decreased bone density, diminished adult height, and impaired spatial memory (Hembree et al., 2017; Hruz, 2020).

Table 37.5 is a drug prototype table for GnRH analogs featuring leuprolide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class GnRH agonist **Mechanism of Action** Decreases testosterone production and lessens the development of male secondary sex characteristics	**Drug Dosage** 3.75–7.5 mg intramuscularly monthly.
Indications Aids in MTF transition **Therapeutic Effects** Suppresses puberty and development of secondary sex characteristics	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Information is inconclusive; may cause the following: Decreased bone density Impaired fertility Hot flashes Acne Emotional lability Cognitive issues Prolonged QT/QTc interval or other cardiac issues (irregular rhythms, heart failure)	**Contraindications** Hypersensitivity History of thrombotic events Hormone-sensitive cancers Hyperglycemia and increased risk for diabetes Prepuberty (client should reach Tanner stage 2 before using the drug)

TABLE 37.5 **Drug Prototype Table: Leuprolide** (sources: https://dailymed.nlm.nih.gov/dailymed/; Unger, 2016)

Finasteride

Finasteride is a 5-alpha-reductase inhibitor essential for the development of male sex characteristics before birth, such as the formation of external genitalia. It acts to inhibit the conversion of testosterone to 5-alpha-dihydrotestosterone. Finasteride does not block the production or action of testosterone. Thus, it has less antiandrogenic effect than spironolactone does (DailyMed, *Finasteride*, 2018; T'Sjoen et al., 2019). However, it is a good choice for individuals who are unable to take spironolactone because of contraindications or other physiologic concerns or who lack the finances or insurance coverage to obtain spironolactone (Deutsch, 2016; Unger, 2016).

The therapeutic effects of finasteride in the context of MTF transition are the same as the adverse effects when it is used for male pattern hair loss. It results in decreased libido, decreased ejaculation, erectile dysfunction, and breast enlargement. The daily dose is 1–5 mg orally. Finasteride has no confirmed drug or food interactions (DailyMed, *Finasteride*, 2018); T'Sjoen et al., 2019; Unger, 2016).

SAFETY ALERT

Finasteride

Females of childbearing age, particularly those who are pregnant, should not handle finasteride, especially if the tablets are broken. The medication can be absorbed and negatively affect genital development in a male fetus.

Adverse Effects and Contraindications

Finasteride is contraindicated for use in female clients and during pregnancy. Additionally, those who are pregnant should not handle crushed or broken pills because finasteride can cause abnormalities of the external genitalia in a male fetus. Adverse effects may include breast tenderness, testicular pain, depression, breast cancer, and liver toxicity (DailyMed, *Finasteride*, 2018; Unger, 2016).

Table 37.6 is a drug prototype table featuring finasteride. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class 5-alpha-reductase inhibitor **Mechanism of Action** Inhibits the conversion of testosterone to 5-alpha-dihydrotestosterone	**Drug Dosage** 1–5 mg orally daily.
Indications Aids in MTF transgender transition **Therapeutic Effects** Shrinking of prostate gland Decreased libido Erectile dysfunction Decreased volume of ejaculate Breast enlargement	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Breast tenderness Testicular pain Breast cancer Depression Liver toxicity	**Contraindications** Females Pregnancy Children Caution: Liver disease because the drug is metabolized in the liver

TABLE 37.6 **Drug Prototype Table: Finasteride** (sources: https://dailymed.nlm.nih.gov/dailymed/; Deutsch, 2016)

CLINICAL TIP

Target for Hormone Therapy

A reasonable target for hormone therapy for transgender female clients is to reduce testosterone levels to the typical range of 30–100 ng/dL found in cisgender female individuals without producing an above-normal level of estradiol (less than 200 pg/mL). This is accomplished by administering an antiandrogen and estrogen.

(Source: Boston University, n.d.)

Nursing Implications

The nurse should do the following for clients who are taking feminizing hormones:

- Assess baseline health, including underlying medical conditions, current medications, and pertinent laboratory and diagnostic results.
- Be cognizant of the client's feelings, values, and culture in order to render sensitive care.
- Monitor for feminizing and adverse effects every 3 months for the first year and then every 6–12 months and as needed for problems.
- Monitor serum testosterone and estradiol levels at follow-up visits, with a practical target in the female range (testosterone, 30–100 ng/dL; estradiol, less than 200 pg/mL).
- Monitor prolactin and triglyceride levels before the client starts hormone therapy and at follow-up visits.
- Monitor potassium levels if the client is taking spironolactone.
- Perform bone mineral density screening before the client starts hormone therapy if they are at risk for osteoporosis. Otherwise, start screening at age 60 or, if sex hormone levels are consistently low, earlier.
- Screen MTF clients for breast and prostate cancer appropriately.
- Ensure that the client understands issues related to family planning and has had an opportunity to meet with a family planning specialist to discuss options because of the fertility-related effects of these drugs. Resources are available for various options, such as freezing sperm or donating sperm to a partner or another person who will carry a pregnancy.

- Ensure that the client is aware of and has access to resources such as community organizations, specialty clinics and hospitals, and support groups.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a feminizing hormone should:

- Know the names, actions, effects, side effects, contraindications, precautions, and drug and food interactions related to their medications.
- Understand the schedule for medication administration: time, dosage, and route.
- Understand the importance of keeping all medications away from children.
- Be able to self-administer parenteral or transdermal medications.
- Notify the health care provider regarding any serious or particularly uncomfortable adverse effects, including hives, swelling of the lips or mouth, severe mood changes, irregular heart rhythm, muscle cramps, and seizures.
- Be aware of fertility considerations and the available options.
- Continue to attend wellness visits and schedule routine diagnostic procedures such as for prostate and breast cancer prevention.
- Be aware of community resources for transgender individuals such as health care and support groups.

SPECIAL CONSIDERATIONS

Resources

These resources may be helpful for transgender, nonbinary, and LGBTQ+ clients:

- American Bar Association Transgender Resources (https://openstax.org/r/americanbar)
- GLAAD (https://openstax.org/r/glaadorg)
- Human Rights Campaign (https://openstax.org/r/hrcorgre)
- National Center for Transgender Equality (https://openstax.org/r/transequalityo)
- Trans Lifeline (https://openstax.org/r/translifelineo)

In addition to these online resources, most campuses have a diversity center open to all students. Larger teaching hospitals often have resources for clients who are experiencing gender issues. Public health entities, such as local health departments, also may have assistance available.

LINK TO LEARNING

Intersex Documentary

Access multimedia content (https://openstax.org/books/pharmacology/pages/37-2-feminizing-hormonal-therapy)

The documentary *Secret Intersex* explores the lives of individuals who were born with ambiguous genitalia or other sexual characteristics. Parents must choose how to raise their children and decide whether and when to pursue medical treatment such as hormone therapy and surgery.

37.3 Masculinizing Hormonal Therapy

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 37.3.1 Identify the characteristics of masculinizing hormonal drugs used for transgender and nonbinary therapy.
- 37.3.2 Explain the indications, actions, adverse reactions, and interactions of masculinizing hormonal drugs used for transgender and nonbinary therapy.
- 37.3.3 Describe nursing implications of masculinizing hormonal drugs used for transgender and nonbinary therapy.
- 37.3.4 Explain the client education related to masculinizing hormonal drugs used for transgender and nonbinary therapy.

The hormones used for reproductive health, covered in Reproductive Health Drugs, are also discussed in this chapter; complete information for the drugs can be found there. Discussion in this chapter focuses on use of the medications to develop male secondary sex characteristics in individuals who were assigned female at birth and choose to undergo female-to-male (FTM) transition. Further transition would include chest masculinization surgery, hysterectomy, and creation of external male genitalia (Mount Sinai, n.d.-a).

The overall effects of masculinizing hormonal drugs on the female body include the growth of facial hair and increased body hair, deepening of the voice, redistribution of subcutaneous fat, increased muscle mass, hairline recession, and, possibly, male pattern baldness (Figure 37.3). Sexual and gonadal effects include an increase in libido, clitoral growth, vaginal dryness, and cessation of menses (Deutsch, 2016; Hembree et al., 2017; Mayo Clinic, 2021b; Unger, 2016).

Although male hormone therapy produces some of the secondary male characteristics in females who are transitioning to males, it also has adverse effects that may be problematic. Possible complications include weight gain, acne, male pattern baldness, sleep apnea, elevated cholesterol, hypertension, polycythemia, type 2 diabetes, infertility, deep vein thrombosis, pulmonary embolism, increased risk for heart disease, drying and thinning of the vaginal lining, pelvic pain, and clitoral discomfort (Mayo Clinic, 2021b).

One major consideration for any transgender male is the danger the hormones pose to a fetus. Testosterone in particular is teratogenic, but other hormones are as well (Rodriguez-Wallberg et al., 2022). Thus, the nurse must ensure that a female client transitioning to male has had a negative pregnancy test.

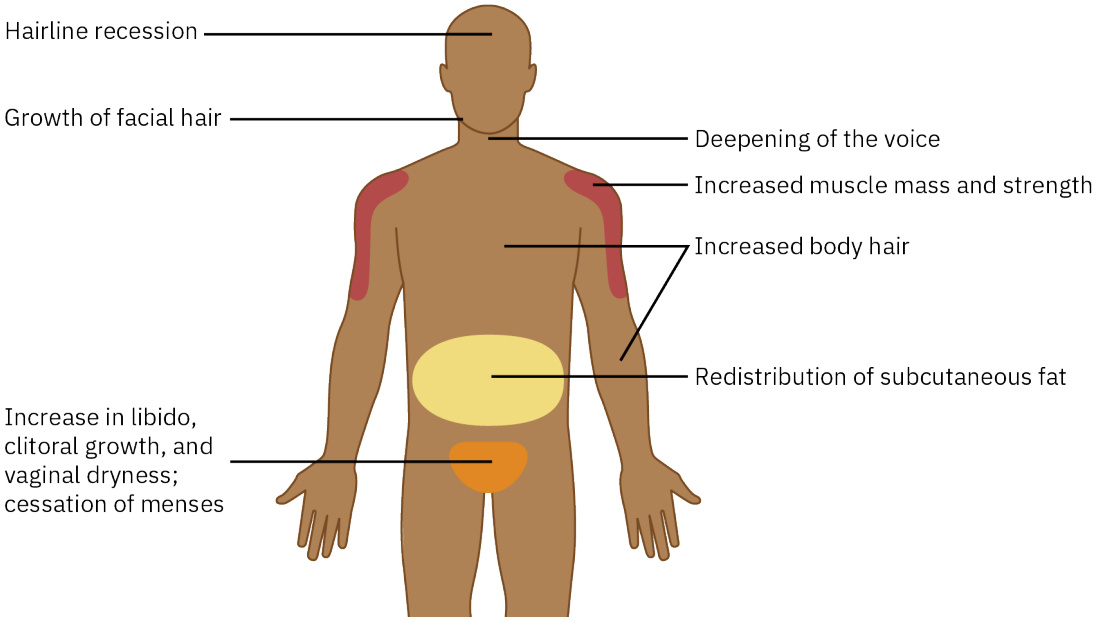


FIGURE 37.3 Drugs used for female-to-male transition affect many areas of the body. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Androgens

Androgens are a group of male hormones, including testosterone. They can be endogenous (produced in the body) or synthetic (developed in a laboratory). All forms of androgens assist with the development of male secondary sex characteristics (Deutsch, 2016; Hembree et al., 2017; Mayo Clinic, 2021b; T'Sjoen et al., 2019; Unger, 2016). In the case of FTM transition, synthetic androgens must be administered exogenously because the female body does not produce them.

Androgens increase the retention of nitrogen, sodium, potassium, and phosphorous and decrease the urinary excretion of calcium. Therefore, a female client transitioning to male should be evaluated for any underlying condition that would be affected by increased levels of these electrolytes, primarily cardiac and renal disorders (DailyMed, *Testosterone cypionate,* 2018).

SAFETY ALERT

Androgens and Diabetic Medication

Androgens can decrease blood glucose levels in clients with diabetes. Dosages of insulin and other hypoglycemic medications must be monitored and possibly decreased to prevent dangerous hypoglycemic events.

(Source: DailyMed, *Testopel*, 2018)

Danazol

Danazol is a synthetic androgen that inhibits pituitary gonadotropins and in turn suppresses ovarian response to the pituitary. Danazol has weak properties and acts similarly to testosterone. In females it causes masculinization effects. Generally, the pituitary-suppressive action of danazol is reversible.

Contraindications to danazol include hypersensitivity; undiagnosed abnormal genital bleeding; markedly impaired hepatic, renal, or cardiac function; pregnancy; breastfeeding; androgen-dependent tumor; and active thrombosis or thromboembolic disease or a history of such events. Danazol may cause some fluid retention, so it should be used cautiously in clients with conditions that may be affected by excess fluid, including epilepsy, migraine, cardiac or renal dysfunction, polycythemia, and hypertension. Danazol should also be used with caution inclients with diabetes (DailyMed, *Danazol*, 2023).

Testosterone

Testosterone is a hormone responsible for the development of male sex organs and secondary sex characteristics. These characteristics include the male pattern of hair distribution (pubic area, axillae, face, and chest), deepening of the voice, heavier bone structure, increased hematocrit, and differences in fat distribution (T'Sjoen et al., 2019). Testosterone undecanoate is an androgen and anabolic steroid medication used mainly to treat low testosterone levels in male clients. It is also used to promote secondary sex characteristics in females transitioning to males (DailyMed, *Aveed*, 2021; T'Sjoen et al., 2019).

A realistic target for hormone therapy for FTM transition is to administer testosterone until testosterone levels are within the typical male physiologic range (320–1000 ng/dL).

Table 37.7 lists common forms of testosterone and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Testopel pellet	75 mg subcutaneous implant (6 pellets implanted every 3–4 months).
Testosterone enanthate (Delatestryl) Testosterone cypionate (Depo-Testosterone)	50–100 mg intramuscularly/subcutaneously weekly or 100–200 mg intramuscularly every 2 weeks.
Testosterone gel	50–100 mg daily.

TABLE 37.7 **Drug Emphasis Table: Testosterone** (sources: https://dailymed.nlm.nih.gov/dailymed/; Coleman et al., 2022)

Drug	Routes and Dosage Ranges
Testosterone patch (AndroGel, Androderm)	2.5–7.5 mg daily transdermally.
Testosterone undecanoate	1000 mg intramuscularly every 12 weeks or 750 mg intramuscularly every 10 weeks.

TABLE 37.7 **Drug Emphasis Table: Testosterone** (sources: https://dailymed.nlm.nih.gov/dailymed/; Coleman et al., 2022)

Fluoxymesterone and Methyltestosterone

Fluoxymesterone and methyltestosterone are anabolic steroids. Their use in FTM transition is to assist in the development of secondary male sex characteristics. Contraindications and precautions include pregnancy; diabetes; and liver, renal, or cardiac disease. Adverse effects include acne, heart or blood vessel problems, stroke, liver problems, mental or mood problems, and infertility. For more information regarding anabolic steroids, see Reproductive Health Drugs.

Progesterone

Progesterone has some minor anabolic and adrenergic properties that can help with development of male characteristics (increased hair growth) and suppression of female characteristics (decreased breast size). See Reproductive Health Drugs for more information about progesterone. For individuals who do not want therapies that contain estrogen, are at risk for thromboembolic complications, or have other contraindications, progesterone is an alternative to estrogen.

CLINICAL TIP

Target for Hormone Therapy

A practical target for hormone therapy for FTM transition is to administer testosterone until testosterone levels reach the typical cisgender male physiologic range (320–1000 ng/dL).

(Source: Hembree et al., 2017)

Table 37.8 is a drug prototype table for masculinizing hormones featuring the testosterone patch. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Masculinizing hormone **Mechanism of Action** Suppresses estrogen and enhances testosterone	**Drug Dosage** 2.5–7.5 mg daily transdermally.
Indications For use in FTM transgender transition **Therapeutic Effects** Increased muscle mass Increased body hair Increased libido Voice deepening Cessation of menses	**Drug Interactions** Oral anticoagulants Hyperglycemic drugs (doses may need to be decreased because the testosterone patch may decrease blood glucose levels inclients with diabetes) Corticosteroids **Food Interactions** No significant interactions
Adverse Effects Application site pruritus, blistering, erythema Back pain Headache Depression Gastrointestinal bleeding Acne Pelvic pain Decreased libido	**Contraindications** Pregnancy Presence of a hormone-sensitive cancer History of blood clots (deep vein thrombosis or pulmonary embolism) Serious cardiac, hepatic, or renal disease Significant mental health conditions, such as severe depression or psychosis, that have not been addressed

TABLE 37.8 **Drug Prototype Table: Testosterone Patch** (sources: https://dailymed.nlm.nih.gov/dailymed/; Coleman et al., 2022)

Nursing Implications

The nurse should do the following for clients who are taking masculinizing hormones:

- Assess baseline health, including underlying medical conditions, current medications, and pertinent laboratory and diagnostic results.
- Be cognizant of the client's feelings, values, and culture in order to render sensitive care.
- Be knowledgeable about drug actions, side effects, contraindications, and precautions and assess the client's knowledge and understanding.
- Obtain a hematocrit and lipid profile before the client starts hormone therapy and at follow-up visits.
- Monitor virilizing and adverse effects every 3 months for the first year and then every 6–12 months.
- Assess serum testosterone at follow-up visits, with a practical target in the male range of 400–700 ng/dL. Peak levels for clients taking parenteral testosterone can be measured 24–48 hours after injection. Trough levels can be measured immediately before injection.
- Screen for bone mineral density before clients at risk for osteoporosis start hormone therapy. Otherwise, screening can start at age 60 or, if sex hormone levels are consistently low, earlier.
- Screen clients with cervixes or breasts appropriately.
- Ensure that the client understands issues related to family planning and has had an opportunity to meet with a family planning specialist. Resources are available for various options, such as freezing eggs or donating eggs to a partner or gestational surrogate.
- Ensure that the client is aware of and has access to resources such as community organizations, specialty clinics and hospitals, and support groups.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a masculinizing hormone should:

- Know the names, actions, effects, side effects, contraindications, and precautions related to each medication.
- Understand the schedule for medication administration—time, dosage, and route.
- Know how to self-administer parenteral or transdermal medication.
- Be aware of drug–drug, drug–food, and drug–herbal interactions as indicated for specific drugs, such as testosterone and warfarin and diabetes medications.
- Notify the health care provider if any of the following occur:
  - Serious reactions to any drug, including swelling of the mouth, lips, or tongue; respiratory problems; or skin rash
  - Any adverse effect that becomes too uncomfortable (e.g., clitoral enlargement, acne)
  - New onset of diabetes or a thyroid disorder; substantial weight changes; subjective or objective evidence of regression of virilization; or new symptoms potentially precipitated or exacerbated by hormone imbalances, such as hot flashes, pelvic cramping, or bleeding
- Be aware of fertility considerations and the available options.
- Continue to attend wellness visits and schedule routine diagnostic procedures such as for prostate and breast cancer prevention.

LINK TO LEARNING

Scholarly Articles

- This article from the journal *Brain* discusses the role of the brain in determining sex and gender identity (https://openstax.org/r/doiorg10.093brain).
- This article from the *International Journal of Environmental Research and Public Health* explores the feelings of nonbinary individuals who encounter the health care system (https://openstax.org/r/trulylistento).

FDA BLACK BOX WARNING

Danazol

Danazol can result in androgenic effects on the female fetus. If a client becomes pregnant while on therapy, the drug should be discontinued. A pregnancy test is required before clients of childbearing age begin therapy, and a nonhormonal method of contraception should be used during therapy.

Testosterone

Virilization has been reported in children who were secondarily exposed to **topical testosterone** gel/solutions. Children should avoid contact with adult application sites for these products.

Serious reactions, involving urge to cough, dyspnea, throat tightening, chest pain, dizziness, syncope, and episodes of anaphylaxis, have been reported to occur during or immediately after the administration of **testosterone undecanoate** injection. This product is available through a REMS program and requires that clients be observed in the health care setting for 30 minutes in order to provide appropriate medical treatment in the event of serious reactions or anaphylaxis.

Testosterone enanthate (subcutaneous) and **testosterone undecanoate** (oral) can cause blood pressure increases that can increase the risk for major adverse cardiovascular events, including nonfatal myocardial infarction, nonfatal stroke, and cardiovascular death, especially in clients with cardiovascular risk factors or established cardiovascular disease. Before initiating testosterone enanthate, consider the client's baseline cardiovascular risk and ensure blood pressure is adequately controlled. Additionally, blood pressure should be monitored throughout the treatment period and risk versus benefits evaluated for clients who develop cardiovascular risk factors or disease while on treatment.

Chapter Summary

This chapter began by defining terms used to describe the transgender and nonbinary population. The terms overlap and can have different meanings depending on the individual's preference and culture, societal norms, and the historical meaning of the terms. The nurse who cares for transgender and nonbinary clients should determine which terms are appropriate or preferred for each client. The chapter listed several websites as resources for both clients and health care professionals. The websites define terms, explore issues related to transgender and nonbinary individuals, and present information on community organizations that provide support.

This chapter covered the medications used by some transgender and nonbinary individuals. Although typical health conditions can be part of the health care needs of this population, the chapter specifically focused on hormonal and other medications used for individuals transitioning partially or completely into a gender opposite the sex assigned at birth or for individuals who do not identify with one gender. One learning tip that can help the reader is to recognize that the hormonal drugs in this chapter are the same as those in Reproductive Health Drugs. Thus, the content is not new, but the application is different. Side effects of male hormones become the intended or therapeutic effects when used in FTM transgender transition treatment, and vice versa.

The medications were divided into two sections: feminizing hormones and masculinizing hormones. This classification does not mean that gender transitioning can only be one or the other; it was just intended to simplify the sections for readers, with the caveat that clients need to be treated on an individual basis.

Above all, nurses who care for clients who are transgender, nonbinary, or do not fit society's traditional ideas of what is acceptable must face their own biases and preconceptions. These clients deserve respect and compassion.

Key Terms

cisgender individuals whose sex assigned at birth and gender identity are congruent

gender dysphoria a deep sense of unease, anxiety, or discomfort that may occur in people whose gender does not align with their sex assigned at birth

gender expression ways in which a person outwardly expresses their gender identity

gender fluid a person who does not identify with a single fixed gender or has a changing or unfixed gender identity

gender identity a person's deeply held beliefs about who they are from a sexual perspective and with which, if any, gender they identify

gender nonconforming a gender presentation that is outside the typical binary presentation; it can also define an individual who identifies outside the man–woman binary.

gynecomastia a condition in which male breast tissue becomes enlarged and overdeveloped

nonbinary an individual whose gender identity does not fit into the man–woman dichotomy

transgender a broad term used by individuals whose sex assigned at birth does not match the gender they feel they are

transsexual a term that sometimes may be used interchangeably with *transgender* to indicate an individual whose sex assigned at birth and gender identity do not match

Review Questions

1. During an assessment interview, a client reveals they are nonbinary. Which action is the most important one for the nurse to take when working with this client?

a. Self-assess personal attitudes toward nonbinary individuals
b. Review the client's childhood history for possible sexual abuse
c. Encourage discussion of the client's aversion to heterosexual relationships
d. Explore the client's family history of gender identity

2. The nurse is describing the intended effect of estrogen therapy to a client who is undergoing male-to-female transition. Which statement by the client indicates understanding?

a. "Estrogen will increase my libido."
b. "Estrogen will increase my muscles."
c. "Estrogen will start increasing my breast growth."

d. "Estrogen will cause my voice to sound higher."

3. The nurse in a clinic for transgender individuals is assessing a client transitioning from female to male who is to begin testosterone therapy. Which condition would allow the client to begin taking testosterone, although with caution?
   a. Pregnancy
   b. Hyperlipidemia
   c. Endometrial cancer
   d. Estrogen receptor–sensitive breast cancer

4. The nurse is assessing a client who wants to undergo male-to-female transition hormonal therapy with spironolactone. Which client condition should the nurse explore further?
   a. Overweight
   b. Depression
   c. Hypertension
   d. Asthma

5. A client undergoing MTF transition has been prescribed the antiandrogen medication spironolactone. Which statement by the client indicates understanding of the adverse effects?
   a. "I may notice my voice is getting deeper."
   b. "I should report any irregular heart rhythm and muscle cramps."
   c. "This drug may cause facial hair growth."
   d. "I need to eat foods high in potassium."

6. A male client is on finasteride therapy. He has a teenage daughter who lives with him. Which statement by the client indicates a need for more teaching?
   a. "It's OK for my daughter to put this medication in my pill box."
   b. "This drug won't cause problems with anything I eat."
   c. "This medication will help increase my breast size."
   d. "My sex drive will likely decrease with this medication."

7. A transgender client comes to the clinic to start initial FTM-transition hormone therapy with testosterone. Which laboratory test does the nurse recognize as being the most important one to do before starting therapy?
   a. Pregnancy test
   b. Hematocrit
   c. Triglyceride level
   d. Liver enzyme levels

8. The nurse caring for a client transitioning from female to male who has not undergone gender-affirming surgery teaches the client about maintaining regular health care checks. Which statement is correct to include?
   a. The client can base the physical exam on their perceived gender.
   b. The nurse should recommend cervical and breast cancer screening.
   c. Regular prostate screenings need to be scheduled after age 40.
   d. Annual testing for HIV should be done.

9. An 18-year-old male comes to a transgender clinic. The client says they feel like a woman and have thought about transitioning gender but are still uncertain. The nurse expects which hormone would be the most appropriate for this client?
   a. Estrogen
   b. Prolactin
   c. Testosterone

d. Spironolactone

10. A client transitioning from female to male is taking an androgen, and the nurse is concerned that one of their current medications may need to have the dosage adjusted. Which medication is the nurse most likely concerned about?

a. Metoprolol
b. Insulin
c. Estrogen
d. Bupropion

CHAPTER 38
Ophthalmic Drugs

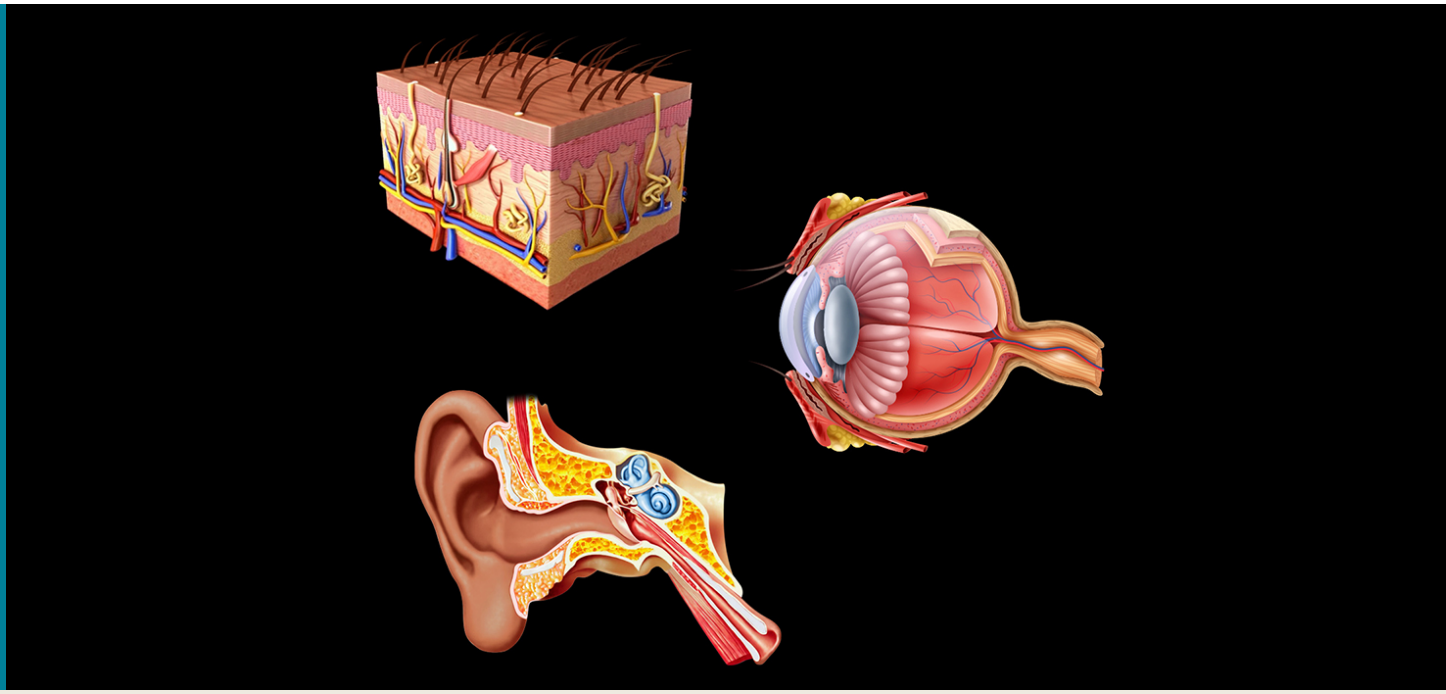


FIGURE 38.1 Maintaining clients' health can include understanding pharmacological options that enhance vision, auditory health, and skin wellness. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The eye is a major sensory organ through which a person obtains information about the external environment. Furthermore, examination of the inner eye can provide information about systemic conditions, such as hypertension or diabetes mellitus. It is essential to recognize the structures and functions of the eye to help facilitate understanding about ocular drug therapy. This chapter begins by introducing the complex structures of the eye along with their functions. It then discusses various ocular disorders, such as refractive disorders, local ophthalmic infections or inflammation, and treatment of glaucoma.

38.1 Introduction to the Eyes

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 38.1.1 Describe the structures and functions of the eyes.
- 38.1.2 Differentiate between glaucoma and other ocular disorders.

Eye Structures and Functions

The human eye is an extension of the brain. Diseases of the brain are sometimes diagnosed by abnormalities seen in the eye. There are eye symptoms that can be benign or progress with age, such as **cataracts**, whereas other ocular symptoms can be red flags for neurological conditions.

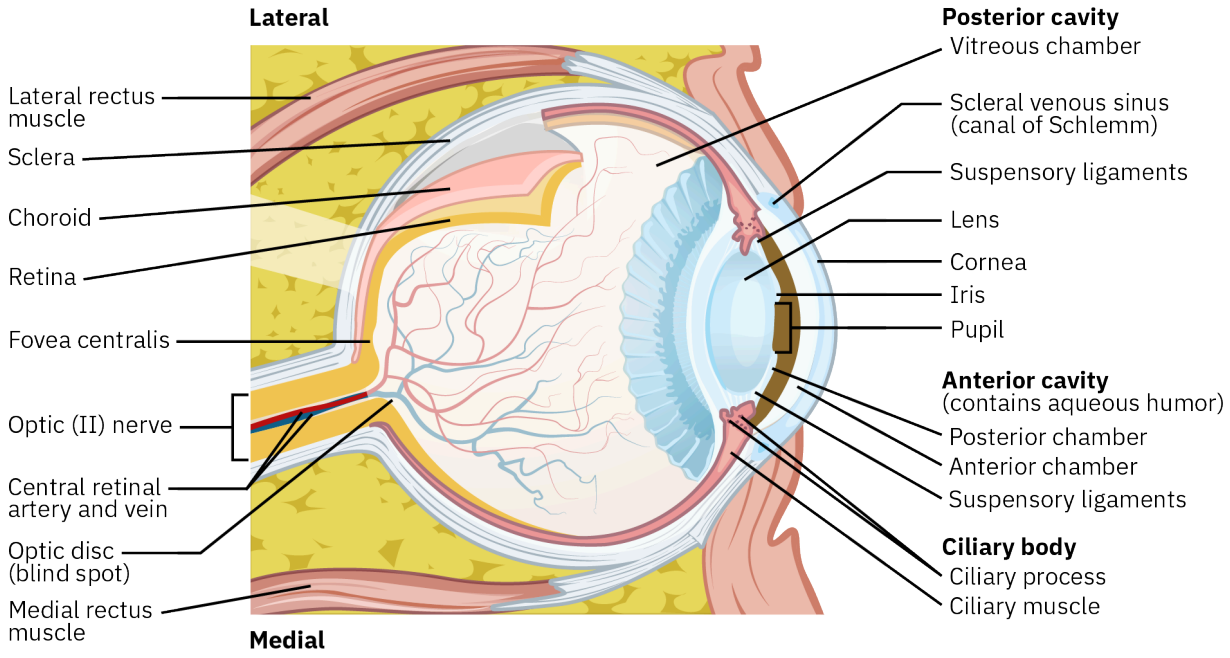


FIGURE 38.2 The eye is a complex sensory organ that contains many structures. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The eye consists of internal and external structures (see Figure 38.2). **Internal ocular structures** include (Garrity, 2022b; Rehman et al., 2022):

- *Pupil:* Allows light to enter the eye, sends neural signals, and begins the process of sight. The pupil is the round black opening in the middle of the iris that responds to light by constricting when light enters and dilating when light is reduced.
- *Iris:* The color of the eye surrounding the black pupil. The iris controls the size of the pupil based on the amount of light. This is an essential nursing assessment because deviations from normal size or unequal size pupils can indicate pathology.
- *Sclera:* The "white of the eye." The sclera helps maintain the eye's shape and functions as a protective layer from injury.
- *Anterior chamber:* Located between the back of the cornea and front of the lens, this chamber contains **aqueous humor**, which is the tissue fluid of the eye. The fluid provides continuous nourishment to the lens and cornea because they have no capillaries of their own.
- *Posterior chamber:* An extension of the anterior chamber located between the lens and retina that contains vitreous humor. This has a gel-like consistency that can thin as one ages and lead to a retinal breach (American Society of Retina Specialists, 2023).
- *Macula:* Responsible for central vision and produces the clearest visual detail.
- *Fovea:* A small depression in the macula and the area for central vision where visual acuity is the highest.
- *Lens:* A transparent structure that lies directly behind the pupil and transmits and focuses light to form images on the retina and for **accommodation** purposes. It is attached to the ciliary muscle.
- *Optic nerve:* The second cranial nerve; it has sensory functions and transmits electrical impulses from the retina to the brain's visual cortex, which displays them as a visual representation.
- *Retina:* The innermost nerve layer, containing microscopic photoreceptor cells to detect light. These receptors are called rods and cones. **Rods** are the receptors for night vison and help with peripheral vision. **Cones** are for daytime vision; they help with central vision and can detect color as well. There are three distinct types of cones, each sensitive to a different color: red, green, or blue.

Intraocular pressure (IOP) is the fluid pressure caused by the amount of aqueous humor in the anterior chamber. A normal IOP is 10–21 mm Hg (Begum, 2023). The pressure is maintained by having the same amount of fluid come in as the amount of fluid leaving the front of the eye. Excess IOP is an important risk factor for glaucoma. Untreated

elevated IOP can lead to blindness. Abnormally low IOP, known as hypotony, can lead to eye wasting.

External ocular structures (see Figure 38.3) include (Garrity, 2022a):

- *Eyelids and eyelashes:* These protect the eye, acting as barriers against foreign bodies, bright light, and small irritants, such as dust.
- *Conjunctiva:* The mucous membrane lining the eyelids. When this becomes inflamed, it is referred to as conjunctivitis, which is caused by allergies, certain bacteria, or viruses.
- *Cornea:* An avascular tissue barrier that protects the eye and will result in blurry vision if scratched. The cornea is the main structure that bends light entering the eye to allow the eye to focus clearly on an image. Refraction errors can manifest as nearsightedness, farsightedness, and astigmatism (described further later in this section).
- *Extrinsic muscles of the eye:* There are a total of six, and they are attached to the bony orbit and to the surface of the eye. There are four rectus muscles (lateral, medial, superior, and inferior) that move the eye up and down or side to side. The two oblique muscles (superior and inferior) rotate the eyes.

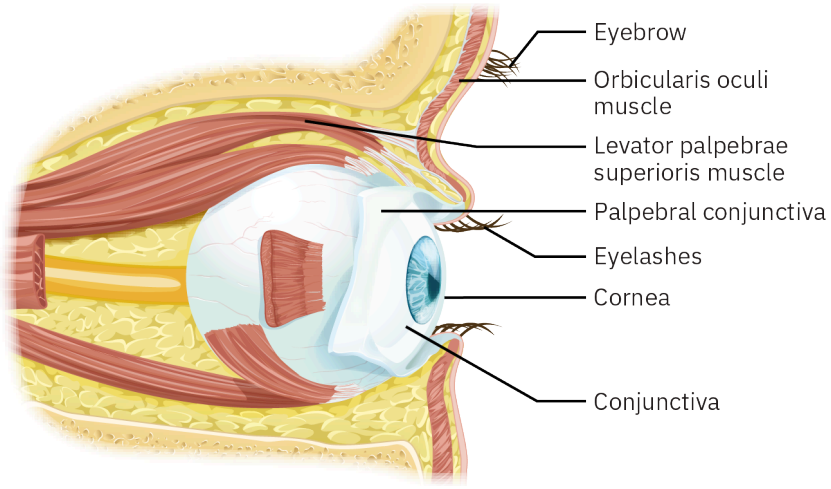


FIGURE 38.3 The external ocular structures help protect the eye. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Fluid is produced by the lacrimal gland located at the upper, outer corner of the eye. This fluid flows continuously, but the amount increases due to irritation and certain emotions. Small lacrimal ducts take the fluid to the anterior surface of the eye. When a person blinks, the fluid spreads, which moistens and washes the surface of the eye. The fluid also contains an enzyme called lysozyme that can inhibit growth of bacteria on the surface of the eye.

There are two small openings at the medial canthus, which is the corner of the eye near the nose. These take the fluid to the lacrimal sac that leads to the nasolacrimal duct. Here the fluid empties into the nasal cavity. This is the reason that noses run when a person cries. If the increase in fluid exceeds the capacity of the drainage system, the excess fluid overflows the eyelids and becomes tears. This is known as lacrimation.

Eye Disorders

Healthy vision requires three basic components: formation of retinal images, stimulation of rods and cones, and nerve impulse conduction to the brain. Malfunction of any of these can disrupt vision. Eye disorders range from common refractive errors that can be treated with the use of eyeglasses, contact lenses, or surgery to more serious conditions such as glaucoma, macular degeneration, and ocular inflammation and infection.

Topical ophthalmic agents play a prominent role in managing many eye disorders. These drugs are intended for direct administration into the conjunctiva of the eye. This route limits systemic absorption, thereby decreasing the risk of adverse effects. Various eye disorders will be addressed in this section. The following section will discuss relevant drugs for specific eye conditions.

Refractive Errors

Refraction of light rays is the deflection or bending of rays as they pass through one object and into another of greater or lesser density. **Refractive errors** occur when the shape of the eye keeps light from focusing directly on

the retina, thereby distorting how objects are seen. When looking at a distant object, the ciliary muscle is relaxed, causing the lens to have a flat shape. If looking at a near object, the ciliary muscle contracts, causing the lens to have a convex shape. The lens should be able to quickly adjust from far to near vision and vice versa. It is the only adjustable structure within the refractory system.

Errors in refraction can be addressed with surgical and nonsurgical interventions. In some cases, a vision prescription can correct how light is refracted on the retina (National Eye Institute, 2022). There are four main refractive errors:

- **Hyperopia**, referred to as farsightedness, is characterized by seeing close objects out of focus; however, distant objects are clearly seen. The light refracts behind the retina to cause this distortion. This is because the eyeball is too short or the lens is too thin.
- **Myopia**, referred to as nearsightedness, is characterized by seeing distant objects out of focus; however, close objects are clearly seen. The light refracts in front of the retina to cause this distortion. This is because the eyeball is too elongated or the lens is too thick.
- **Astigmatism** occurs when light is focused on multiple points along the retina, rather than just a single point. This occurs when the cornea or the lens has a different shape than normal, often shaped more like a football than a baseball (Boyd, 2022a).
- **Presbyopia** occurs as the eye ages and is characterized by lens thickening and loss of elasticity. This change occurs around age 45. Clients may begin to use over-the-counter reading glasses for close-up reading (National Eye Institute, 2020).

LINK TO LEARNING

Refractive Errors

Access multimedia content (https://openstax.org/books/pharmacology/pages/38-1-introduction-to-the-eyes)
The American Academy of Ophthalmology has a video entitled "Vision Loss and Refractive Error," presented by the University of Wisconsin Department of Ophthalmology and Visual Sciences. It discusses topics such as myopia, hyperopia, astigmatism, and presbyopia.

Glaucoma

Glaucoma is a group of diseases characterized by a decrease in peripheral vision due to an obstruction of aqueous humor that increases IOP, which can damage the optic nerve. This leads to diminished and/or distorted vision. Glaucoma can be an inherited condition or occur spontaneously. Black, Hispanic, and Asian clients have a higher risk for glaucoma. Also at higher risk are clients older than 40 years, those with thinner corneas, those with chronic eye inflammation, and those taking medications that are known to increase eye pressure (Boyd, 2022b).

Multiple parameters are assessed when screening for glaucoma, including:

- *IOP:* Average values are 10–21 mm Hg (Begum, 2023).
- *Corneal thickness:* Measured in microns with an average cornea thickness of 555 microns. Thinner corneas may result in artificially low pressure readings, potentially missing a glaucoma diagnosis. Similarly, thicker corneas may cause artificially elevated pressure readings, potentially creating a false glaucoma diagnosis (Glaucoma Research Foundation, 2022).
- *Optic nerve:* A healthy optic nerve is intact and generally does not show asymmetry or cupping (Waisberg & Micieli, 2021).

CLINICAL TIP

Anxiety Can Affect IOP

The nurse should be aware that a client's anxiety can artificially increase an IOP reading. It is important to acknowledge the client's wariness about the tonometer touching the cornea, but the nurse should reassure the client that a numbing drop is used alleviate any perceived discomfort.

Clients are considered "glaucoma suspects" if they have risk factors for glaucoma, including elevated IOP, optic nerve damage, visual field defect, or a strong family history of glaucoma (Ahmad, 2018).

The two forms of glaucoma are open-angle glaucoma (the most common form) and closed-angle glaucoma. Open-angle glaucoma occurs when the trabecular meshwork becomes occluded and cannot drain the continuous production of aqueous humor. Often there are no early symptoms. Eventually, the client begins to lose peripheral vision (Mayo Clinic, 2022). Open-angle glaucoma typically progresses slowly with small increases in IOP over time. Treatments include ophthalmic drops as well as surgical treatments such as **trabeculectomy**, a glaucoma drainage implant that allows aqueous humor to drain through an artificial bleb (a surgically created hole) into the body for processing, and corneal transplant.

Closed-angle glaucoma progresses suddenly with a sudden rise in IOP. Clients can become blind with little warning. This condition is precipitated by either displacement of the iris or pupil dilation. Both cover the trabecular meshwork, preventing the exit of aqueous humor. IOP increases rapidly to dangerous levels when the angle between the cornea and iris becomes significantly narrowed. Symptoms can include sudden headache, eye pain, and/or blurred vision. Immediate treatment by an ophthalmologic specialist can limit ocular disability by widening the canal of Schlemm in a procedure known as **canaloplasty**.

Macular Degeneration

Macular degeneration occurs when the central portion of the retina inhibits central vision but maintains peripheral vision. Macular degeneration occurs in some clients as the macula ages. There are two types of degeneration:

- Dry macular degeneration (DMD) often has characteristic drusen, which consists of yellow lipid retinal deposits. There is no cure for DMD; however, there is some evidence that various nutritional and vitamin intakes, including vitamin C, lutein, and leafy green vegetables, can slow the progression (American Optometric Association, n.d.; Mrowicka et al., 2022).
- Wet macular degeneration (WMD) is characterized by the growth of new subretinal blood vessels, which are often fragile and leaky. This leakage lifts the macula from its normal place, quickly causing permanent injury. There is no cure for WMD, but it can be treated with laser technology and intraocular medication injections (National Retina Institute, 2023).

Ocular Inflammation and Infection

Ocular inflammation and infection occur when the eye has become inflamed or infected through either illness or injury. **Conjunctivitis**, referred to as pink eye, occurs when the thin layer of tissue in front of the eye becomes irritated and red, often producing a sticky coating on the eyelashes. These symptoms can increase tear production, produce a sensation of a foreign body in the eye, and cause the client to rub their eyes. Conjunctivitis can be caused by a bacterial or viral infection, allergy, or irritant, such as a stray eyelash or after swimming in a chlorinated pool. Bacterial conjunctivitis is often treated with ocular antibacterials, in the form of either an ointment or a solution (Centers for Disease Control and Prevention, 2019). Complications are rare; however, they can include eye scarring or a secondary infection such as meningitis (National Health Service, 2023).

There are numerous other infections and inflammatory conditions of the eye that occur at different ocular anatomical sites, including:

- Episcleritis occurs between the conjunctiva and sclera and has a similar presentation to conjunctivitis (Johns Hopkins Medicine, n.d.; Schonberg & Stokkermans, 2023).
- Keratitis is characterized by corneal inflammation that can cause ulceration. Keratitis is considered a medical emergency. The client will need a timely diagnosis and treatment plan because extensive ulceration can lead to blindness. Keratitis is associated with infectious and noninfectious causes (Singh et al., 2023).
- Uveitis is an inflammation of the middle part of the eye called the uvea. Though infection can be a factor, uveitis is largely considered autoimmune secondary to other systemic diseases such as ankylosing spondylitis and reactive arthritis (Rosenbaum, 2019). Uveitis is characterized by eye pain, eye redness, and **photophobia**. It is essential that the client seek timely diagnosis and treatment with ocular corticosteroids to avoid vision loss.
- A chalazion occurs when meibomian glands become occluded. It presents with edema and pain on the eyelid and is initially treated with warm wet compresses several times per day, but it may also require antibiotics and possible surgical intervention.

- A hordeolum (stye) is a red, painful bump near the edge of the eyelid that looks like a pimple or boil. A stye has an infectious cause and often responds to warm wet compresses. Oral antibiotics are sometimes needed to successfully treat a hordeolum (American Academy of Ophthalmology, 2022).
- Orbital cellulitis is an infection of the fat and muscles around the eye caused by pathogens, trauma, or spreading of infection from the sinuses. Orbital cellulitis can be serious and lead to brain abscess and vision loss. The client may present with a fever, eye pain, and a bulging eye. A dental history should also be reviewed because a dental abscess can track upward into the orbits. Treatment includes broad-spectrum antibiotics until the actual organism can be identified (Satar et al., 2021). Once the organism has been determined, appropriate antibiotics can be started.
- Obstruction or inflammation of the lacrimal gland or the lacrimal sac can occur. When the lacrimal gland is inflamed, this is termed dacryoadenitis. If the lacrimal sac is inflamed, this is referred to as dacryocystitis. Treatment consists of warm compresses, ocular antibacterials, and oral antibiotics as needed. The Crigler massage is sometimes recommended to release material from the affected tear duct by pressing a clean index finger inward against the lacrimal sac and massaging downward toward the nose (Hu et al., 2022).
- Keratoconjunctivitis sicca is dryness of the conjunctiva and cornea. The dry eyes can be the result of too few tears being produced or tears that evaporate too quickly. This condition is characterized by inflammation of the ocular surface and lacrimal glands.

Administration of Ophthalmic Drugs

It is important for the nurse to communicate with the client prior to eye medication administration to set expectations regarding drug indications and administration technique. This helps ensure that the client can participate in ocular medication administration and support medication efficacy.

Administration of Solution or Drops

To properly administer solution or drops, the client should:

1. Check the expiration date prior to administration, and discard if expired.
2. Wash and dry hands thoroughly before administering eye medication.
3. Shake the bottle gently to ensure the medication is evenly distributed, especially if the drug is a suspension.
4. Tilt head back and stare upward so the medication does not directly hit the eyeball.
5. Pull the lower eyelid away from the eye to form a pouch and instill the prescribed number of drops into the conjunctival sac.
6. Release the eyelid slowly.
7. Close the eye and look downward for 1–2 minutes.
8. Apply gentle pressure to the corner of the eye where the upper and lower lids meet closest to the nose for 30–60 seconds to prevent systemic absorption.

The client should wait at least 2 minutes between drops if needing to administer more than one drop of the same medication; they should wait at least 5 minutes between drugs if a different ocular medication is prescribed.

The client *should not*:

- Allow the dropper to touch their eye or any other surface.
- Rub the eyes after administration.
- Rinse the eyedropper.
- Use eye drops that have changed color.
- Wear contact lenses before or several minutes after administration.
- Administer eye drops if they have injured their eye because the drops can cause pain and make the injury worse.

CLINICAL TIP

Geriatric and Pediatric Administration

Older adults or others needing assistance with administration should try a device that can attach to the medication bottle, making it easier to hold the bottle and administer the drops. These products are available at

pharmacies and where medical supplies are sold. If the client's hands shake, they can approach the eye from the side with the hand resting on the side of the face. They can also wrap a cloth or paper towel around the bottle and dropper to make it larger and easier to grip.

For pediatric clients, if possible, have a second person available to help position the child and keep them still during administration. If the child will not open their eyes, place the drops in the inner corner of the eye so when they open their eyes the medication will fall in.

Administration of Ointment

To properly administer ointment, the client should:

1. Wash and dry hands thoroughly before administering eye medication.
2. Hold the tube between their hands for 2–4 minutes to warm the ointment.
3. Tilt their head back and stare upward.
4. Pull the lower eyelid away from the eye to form a pouch.
5. Hold the tube about 1 inch above the eye and place a thin layer of approximately 0.25–0.5 inches inside the lower lid.
6. Close the eyes for 1–2 minutes and roll the eyes around in all directions so the ointment melts and gets dispersed over the entire eye.
7. Wipe away any excess ointment from the eyes.
8. Wait 30 minutes before applying a second ointment (if prescribed).

The client *should not*:

- Rub their eyes after administration.
- Wear contact lenses during treatment, unless told otherwise, because the contact lenses can become damaged.
- Use after the recommended time, to prevent an eye infection.
- Drive or operate heavy machinery. Ointments are thick and can cause transient blurred vision.
- Apply ointment if they have sustained an eye injury because the ointment can cause pain or make the injury worse.

CLINICAL TIP

Combination Prescription for Both Drops and Ointment

Some individuals may have to administer drops and ointment, depending on their prescribed medications. It is crucial the drops are instilled first. The client should then wait 5–10 minutes before applying the ointment. If they do it in the reverse order, the ointment may get washed away and will be ineffective.

LINK TO LEARNING

Instilling Eye Drops and Eye Ointments

Access multimedia content (https://openstax.org/books/pharmacology/pages/38-1-introduction-to-the-eyes)
In the first link to learning, a video entitled "How to Safely Instill Eye Drops," Dr. Brigitte Keener explains and demonstrates the proper way to instill eye drops to ensure safety and effectiveness. The video is presented by the Mayo Clinic.

Access multimedia content (https://openstax.org/books/pharmacology/pages/38-1-introduction-to-the-eyes)
In another video, a practicing pharmacist, Abraham Khodadi, describes and illustrates the correct way to use eye ointment.

38.2 Ocular Anti-inflammatories and Anti-infectives

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 38.2.1 Identify the characteristics of anti-inflammatory and anti-infective drugs used to treat eye disorders.
- 38.2.2 Explain the indications, actions, adverse reactions, and interactions of anti-inflammatory and anti-infective drugs used to treat eye disorders.
- 38.2.3 Describe the nursing implications of anti-inflammatory and anti-infective drugs used to treat eye disorders.
- 38.2.4 Explain the client education related to anti-inflammatory and anti-infective drugs used to treat eye disorders.

Ocular Nonsteroidal Anti-inflammatories

Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to prevent and treat eye inflammation. They can help relieve symptoms of pain and swelling from eye conditions or injuries or after eye surgery. Diclofenac sodium and ketorolac tromethamine are both used to treat postoperative ocular inflammation after cataract extraction. They are also used to treat ocular pain and photophobia in clients undergoing corneal refractive surgery. To manage these conditions, drugs are administered directly into the affected eye(s).

Table 38.1 lists common ocular nonsteroidal anti-inflammatory drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Diclofenac sodium (Voltaren Ophthalmic)	*For postoperative ocular inflammation after cataract extraction:* *0.1% ophthalmic solution:* 1 drop to the affected eye(s) 4 times daily, starting 24 hours after cataract surgery and continuing for 2 weeks after the postoperative period. *For ocular pain and photophobia in clients undergoing corneal refractive surgery:* *0.1% ophthalmic solution:* 1–2 drops to the operative eye(s) within 1 hour before surgery. Within 15 minutes after surgery, apply 1–2 drops to the operative eye(s). Instill 1–2 drops 4 times daily for up to 3 days.
Ketorolac tromethamine (Acular)	*For reduction of postoperative ocular inflammation and ocular pain after cataract surgery or corneal refractive surgery:* *0.5% ophthalmic solution:* 1 drop into the affected eye(s) 4 times daily beginning 24 hours after cataract surgery; continue through the first 2 weeks after surgery. *For the treatment of ocular pruritus due to seasonal allergic conjunctivitis:* *0.5% ophthalmic solution:* 1 drop in the affected eye(s) 4 times daily.

TABLE 38.1 **Drug Emphasis Table: Ocular Nonsteroidal Anti-inflammatories** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Similarly Named Drugs

Do not confuse ketorolac (ocular NSAID) with Ketalar (nonbarbiturate anesthetic).

(Source: Institute for Safe Medication Practices, 2023)

Adverse Effects and Contraindications

Adverse effects are essentially identical for both drugs. Although administering drugs using the ophthalmic route causes minimal systemic effects, they still can occur. The potential exists for prolonged bleeding due to interference with the aggregation (clumping) of thrombocytes (platelets). Blood can enter the aqueous humor, resulting in a hyphema (a collection of blood in the anterior chamber of the eye). The blood usually will dissipate on its own over time. In some susceptible clients, such as those with corneal denervation, dry eye syndrome, diabetes mellitus, or rheumatoid arthritis, continued use of topical NSAIDs over 14 days may result in epithelial breakdown, corneal thinning, erosion, ulceration, or perforation. If any of these occur, they can impair vision. Clients who exhibit evidence of corneal epithelial breakdown should immediately discontinue use of the topical NSAIDs and must be

closely monitored to ensure proper healing of the cornea.

All ophthalmic NSAIDs and corticosteroids may slow or delay healing. Concurrent use of these drugs may increase the potential for further healing difficulties. Combining any ophthalmic NSAID with latanoprost will diminish the therapeutic effect of latanoprost.

Ocular NSAIDs are contraindicated for clients with a history of severe NSAID or acetylsalicylic acid (aspirin) hypersensitivity.

Table 38.2 is a drug prototype table for ocular nonsteroidal anti-inflammatories featuring diclofenac. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Ocular nonsteroidal anti-inflammatory **Mechanism of Action** Inhibits the enzyme cyclooxygenase, which is essential in the biosynthesis of prostaglandins	**Drug Dosage** *Postoperative ocular inflammation after cataract surgery:* 1 drop to affected eye(s) 4 times daily, starting 24 hours after cataract surgery; continue for 2 weeks after the postoperative period. *Ocular pain and photophobia in clients undergoing corneal refractive surgery:* 1–2 drops to operative eye(s) within 1 hour before surgery. Within 15 minutes after surgery, apply 1–2 drops to the operative eye(s). Continue to instill 1–2 drops 4 times daily for 3 days.
Indications Postoperative ocular inflammation after cataract surgery Ocular pain and photophobia in clients undergoing corneal refractive surgery **Therapeutic Effects** Reduces inflammation Reduce intensity of photophobia Relieves symptoms of ocular pain postoperatively	**Drug Interactions** Anticoagulants Antiplatelet aggregators Corticosteroids Latanoprost **Food Interactions** No significant interactions
Adverse Effects Delay in wound healing Keratitis Increased bleeding of ocular tissues from ocular surgery Hyphema Facial edema Fever Dizziness Headache Burning or stinging of the eyes Itchy eyes Blurred vision Fever Lacrimation Corneal opacities or lesions	**Contraindications** Hypersensitivity to NSAIDs or aspirin Pregnancy Breastfeeding Caution: Bleeding conditions (e.g., hemophilia, vitamin K deficiency) Thrombocytopenia Renal insufficiency

TABLE 38.2 **Drug Prototype Table: Diclofenac 0.1% Ophthalmic Solution** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ocular nonsteroidal anti-inflammatories:

- Assess client's visual acuity periodically.
- Monitor for any signs or symptoms of bleeding, especially in the eye.
- Have the client return-demonstrate the application of the drops and/or ointment to ensure they are using the proper technique.
- Encourage the client to get assistance from others or use adaptive devices to minimize the risk of fall or injury until their vision improves.
- Assess for tearing, eye discharge, irritation, and/or facial swelling.
- Monitor severity of pain.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ocular nonsteroidal anti-inflammatory should:

- Notify the provider of any signs or symptoms of keratitis: red eye, sensation of a foreign substance in the eye, eye pain, decreased vision, or sensitivity to light.
- Read the medication label before using; eye medications and ear medications are similarly packaged.
- Avoid contamination of the prescribed product because this can cause infection or damage vision.

The client taking an ocular nonsteroidal anti-inflammatory *should not:*

- Drive or operate machinery until vision clears.

Ocular Immunosuppressants

In ocular inflammation, immunosuppressants are used as steroid-sparing agents to control the inflammation, with a goal of long-lasting remission and prevention of the threat to vision. Likewise, these agents are utilized to "reprogram" the immune system to alleviate or reduce the lymphocytes from attacking and causing recurrent autoimmune destruction of healthy ocular tissue (Liu et al., 2023). Although several drugs could be used, cyclosporine is the predominant one.

Systemic immunosuppressants are used in some cases for inflammatory eye diseases because they can prevent potential permanent vision loss. This treatment strategy is deployed often for uveitis and other ocular conditions when other treatments have failed (Kopplin, 2020).

Adverse Effects and Contraindications

Because there is minimal systemic absorption, most of the adverse effects are local. Hypersensitivity reactions such as ocular redness, blurry vision, and lid swelling can occur; therefore, the client should be aware and observed for signs of this (College of Optometrists, 2023). It is rare for the drug to cause an anaphylactic reaction.

No true contraindications exist when giving this drug via the ophthalmic route. If a client is already immunocompromised from a different condition, it is important for them to contact their provider if they begin to experience signs of infection. If topical corticosteroids are given concurrently with cyclosporine, this can increase the chances of infection because both drugs can decrease the immune response.

Table 38.3 is a drug prototype table for ocular immunosuppressants featuring cyclosporine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Ocular immunosuppressant **Mechanism of Action** Acts as a partial immunomodulator; exact mechanism of action is unknown	**Drug Dosage** *For keratoconjunctivitis sicca:* 1 drop in each eye twice daily, approximately 12 hours apart. Artificial tears may be used concurrently, allowing a 15-minute interval between administration of products.
Indications Treatment of dry eye syndrome due to keratoconjunctivitis sicca **Therapeutic Effects** Increases tear production in clients whose tears are suppressed due to ocular inflammation	**Drug Interactions** Topical corticosteroids **Food Interactions** No significant interactions
Adverse Effects Ocular burning or stinging Blurry vision Hyperemia (redness) of the conjunctiva Eye pain Foreign body sensation Pruritus of eyes Excessive watering of the eyes (epiphora) Hypersensitivity reaction (urticaria, periorbital edema, tongue and pharyngeal edema, along with dyspnea)	**Contraindications** Allergy to any of the ingredients in the drug Caution: Immunocompromised clients Contact lens wearers: Remove contact lens prior to administration

TABLE 38.3 **Drug Prototype Table: Cyclosporine 0.05%** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ocular immunosuppressants:

- Monitor for signs/symptoms of hypersensitivity, such as facial swelling, inflamed tongue, or shortness of breath.
- Ensure the client understands the proper technique for instilling the drop by having them return-demonstrate the procedure.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ocular immunosuppressant should:

- Invert the unit dose vial several times until there is a uniform, white emulsion.
- Use the medication immediately upon opening and discard the remaining solution straightaway.
- Be careful not to touch the tip of the vial to their eye or other surface to avoid the potential for eye injury or contamination.
- Notify the provider of any possible allergic reactions, such as a swollen face, throat, eyes, and/or tongue or shortness of breath.
- Remove their contact lenses prior to instilling the drops. Client can reinsert contacts 15 minutes after administration.
- Wait at least 15 minutes to instill other drops or apply ointments.

Ocular Corticosteroids

Ophthalmic steroids are applied topically for a variety of inflammatory conditions, such as allergic conjunctivitis, uveitis, iritis, and herpes zoster keratitis. In addition, they are beneficial in the treatment of chemical and thermal burns along with foreign body injury. Ophthalmic steroids are also useful in postocular surgery to decrease

inflammation and scar tissue formation. It is best these drugs are used on a short-term basis to minimize adverse effects (Fung et al., 2020). Dexamethasone and prednisolone are the two main drugs used to decrease ocular inflammation.

Dexamethasone

Dexamethasone is a more potent ocular corticosteroid and has a longer duration of action than prednisolone. For ocular use, this drug is available in ophthalmic drops and ophthalmic ointment. It can be used as monotherapy (alone) or in combination with other medications, such as antibiotics. Some dexamethasone dosage forms contain a sulfite that may cause an asthmatic episode or an allergic reaction ranging from urticaria to life-threatening anaphylaxis in those who have a sensitivity to sulfites (DailyMed, *Maxidex*, 2006).

Prednisolone Sodium Phosphate

For ocular use, this drug is available in ophthalmic drops.

Table 38.4 lists common ocular corticosteroids and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Dexamethasone sodium phosphate (Maxidex, Dextenza)	*Ophthalmic dosage for 0.05%, 0.1%, 9%, 0.4 mg, or 0.7 mg:* 1–2 drops into affected eye(s) every hour during the day and every 2 hours during the night as initial therapy. When a favorable response is observed, reduce dosage to 1 drop every 4 hours. Further reduction in dosage to 1 drop 3–4 times daily may suffice to control symptoms.
Prednisolone sodium phosphate (Omnipred)	*Ophthalmic dosage (prednisolone sodium phosphate 1% ophthalmic solution):* 1–2 drops into affected eye(s) every hour while awake and every 2 hours at night. When a favorable response is observed, reduce dosage to 1 drop every 4 hours; thereafter, 1 drop 3–4 times daily to control symptoms. Dosage and duration vary with condition and may extend from a few days to several weeks, according to therapeutic response.

TABLE 38.4 Drug Emphasis Table: Ocular Corticosteroids (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Most of the serious adverse effects occur when the drug is being used for a prolonged period of time. Extended use may cause increased IOP, which may result in glaucoma. Anyone using these products for more than 10 days should routinely have their intraocular pressure checked. In addition, the optic nerve may become damaged, which will cause visual acuity defects and loss of vision in certain fields. Subcapsular cataract formation is also a potential adverse effect. Many viral, bacterial, and fungal infections of the cornea or conjunctiva may be exacerbated; therefore, corticosteroids are contraindicated in those with an active infection (DailyMed, *Prednisolone*, 2023).

If too much drug enters the system, clients on antidiabetic agents or warfarin will need to have their dose adjusted.

Table 38.5 is a drug prototype table for ocular corticosteroids featuring prednisolone. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Ocular corticosteroid **Mechanism of Action** Inhibits inflammatory response to inciting agents of a mechanical, chemical, or immunological nature	**Drug Dosage** *Ophthalmic dosage (prednisolone sodium phosphate 1% ophthalmic solution):* 1–2 drops into affected eye(s) every hour while awake and every 2 hours at night. When a favorable response is observed, reduce dosage to 1 drop every 4 hours; thereafter, 1 drop 3–4 times daily to control symptoms. Dosage and duration vary with condition and may extend from a few days to several weeks, according to therapeutic response.
Indications To decrease inflammation in allergic conjunctivitis, iritis, uveitis, chemical and thermal burns, or deeply penetrated foreign bodies **Therapeutic Effects** Inhibits edema, fibrin deposition, capillary dilation, and leukocyte migration	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Blurred vision Photophobia Eye dryness and/or irritation Cataract formation Glaucoma Optic nerve damage Secondary infection	**Contraindications** Acute superficial herpes simplex keratitis Fungal ocular diseases Acute infectious stages of ocular varicella Viral diseases of the cornea and conjunctiva Tuberculosis of the eye Advanced glaucoma

TABLE 38.5 **Drug Prototype Table: Prednisolone** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ocular corticosteroids:

- Teach the client the proper way to administer the medication and to avoid contamination.
- Assess for therapeutic effects, including decreased eye pain, redness, and irritation.
- Make the environment safe for ambulation because the drug can cause transient blurry vision. Ensure adequate lighting and a clear path to the bathroom.
- Assess for increased eye pain, drainage, headache, prolonged blurred vision or changes in visual acuity, and sensitivity to light.
- Apply warm, wet compresses over affected eye(s) to help reduce inflammation and/or discomfort.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ocular corticosteroid should:

- Follow the tapering instructions given by the prescriber to avoid adrenal gland insufficiency. Usually tapering occurs over a few weeks or months depending on how long steroids were taken.
- Notify their health care provider immediately if they experience excess fatigue, weight loss, increased urine output, confusion, irregular heart rhythm, or dizziness during titration. This may indicate the drug is being stopped too quickly.
- Immediately contact their health care provider if they develop any sudden visual changes, undergo trauma, or develop an infection.
- Wear sunglasses when outside to reduce the sensitivity to light.

The client taking an ocular corticosteroid *should not:*

- Wear contact lenses for at least 15 minutes after instillation of the drug because one of the preservatives in dexamethasone could be absorbed by soft contact lenses, making the drug less effective.
- Drive or participate in hazardous activities until their vision is clear.

Ocular Antibacterials

Topical antibacterials are used to treat ophthalmic infections and to prevent infection after ocular surgery. Bacterial infections are and will remain contagious until treated for 24–48 hours. There are various antibacterials that have ophthalmic uses. These agents are active against numerous gram-positive and gram-negative organisms. They are generally used to treat infections involving the conjunctiva or cornea, such as conjunctivitis, keratitis, corneal ulcers, and blepharitis. The choice of antibiotic depends on the pathogen causing the infection. Additionally, many different combination preparations are available. Caution should be exercised when administering these products with regard to the select agent, strength, and formulation. Unfortunately, the risk of superinfection is high when using ophthalmic antibiotics due to contamination of the eyedropper or tube. Counseling on the proper technique of administration is a critical teaching point to help reduce the risk of superinfection.

Various drug classifications are used to treat ocular infections. Some of these include fluoroquinolones (ciprofloxacin), aminoglycosides (gentamycin, neomycin), macrolides (erythromycin), and a combination drug that includes neomycin. Ocular neomycin can be prescribed in several ways: neomycin, polymyxin B, and bacitracin; neomycin, polymyxin B, and hydrocortisone; neomycin, polymyxin B, and dexamethasone; or neomycin, polymyxin B, and gramicidin. Polymyxin is considered a polypeptide bactericidal antibiotic, while bacitracin is a bactericidal and bacteriostatic polypeptide antibiotic. Dexamethasone and hydrocortisone are corticosteroids (discussed in the previous section). The choice of the medication may depend on many factors. One important factor to consider is whether the client wears contact lenses.

Gentamicin Sulfate

Gentamicin sulfate has bactericidal effects that interfere with bacterial synthesis. This class of medication is used primarily against aerobic gram-negative bacilli, such as *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa.* The drug has no effects on anaerobic bacteria. In addition to the uses of ciprofloxacin, gentamicin can be used for blepharitis, acute meibomianitis (inflammation of the meibomian gland), and dacryocystitis (inflammation of the lacrimal sac) (DailyMed, *Gentamicin*, 2022).

Neomycin Sulfate/Polymyxin B Sulfate/Gramicidin

This combination antibiotic product has multiple mechanisms of action. First, it works similar to gentamicin by interfering with bacterial synthesis. This drug is mainly used in the treatment of bacterial conjunctivitis and blepharitis. Sometimes it is necessary to administer both a corticosteroid and an antibacterial, such as for inflammatory ocular infections or traumas. Even if there is no active infection, corticosteroids reduce the body's immune response, and if this is clinically concerning based on the client's health, an antibacterial may be added as a prophylactic measure.

Erythromycin

This drug is the first-line agent in treating simple cases of bacterial conjunctivitis. It prevents the further growth of bacteria rather than directly destroying them. Interestingly, because this drug is administered via ointment form, even if it stays on the eyelid and eyelashes, it still provides a therapeutic effect despite the medication not being directly on the conjunctiva (DailyMed, *Erythromycin*, 2023).

In newborns born to someone with active disease, 1 cm of ointment is administered one time right after delivery to prevent eye infections, especially gonococcal ophthalmia neonatorum (GON) and chlamydial ophthalmia. If left untreated, these infections can cause serious eye problems, including corneal scarring, ocular perforation, and blindness as early as 24 hours after birth. Erythromycin is the only FDA-approved drug for this purpose.

Table 38.6 lists common ocular antibacterials and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Ciprofloxacin hydrochloride 0.3% (Ciloxan)	*For bacterial conjunctivitis:* *Ophthalmic dosage (ointment):* ½-inch strip of ointment in the affected eye(s) 3 times a day for the first 2 days, then a ½-inch strip in the affected eye(s) 2 times a day for the next 5 days. *Ophthalmic dosage (solution):* 1–2 drops in the affected eye(s) every 2 hours, while awake, for 2 days. Then 1–2 drops in the affected eye(s) every 4 hours, while awake, for the next 5 days. *For corneal ulcers:* *Ophthalmic dosage (solution):* Day 1: 2 drops in the affected eye(s) every 15 minutes for the first 6 hours, and then 2 drops in the affected eye(s) every 30 minutes for the rest of the day, while awake. Day 2: 2 drops in the affected eye(s) every hour, while awake. Days 3–14: 2 drops in the affected eye(s) every 4 hours, while awake.
Erythromycin 0.5% (Ilotycin)	*Ophthalmic ointment:* Approximately 1 cm (less than ½ inch) of erythromycin ophthalmic ointment directly in the affected eye(s) up to 6 times a day, depending on the severity of the infection *Neonatal dosing:* 1 cm of ointment applied to both eyes 1 time following delivery.
Gentamicin sulfate 0.3% (Garamycin)	*Ophthalmic dosage (ointment):* A 1.27-cm ribbon applied to the affected eye(s) 2–3 times a day. *Ophthalmic dosage (solution):* 1–2 drops in the affected eye(s) every 4 hours. For severe infections, use up to 2 drops into the affected eye(s) every hour.
Neomycin sulfate (available only in combination with other drugs for ophthalmic use; specific combination product listed where relevant)	*Neomycin, polymyxin B, and bacitracin:* *Ophthalmic dosage (ointment):* A thin strip of ointment in the affected eye(s) every 3–4 hours for 7–10 days. *Neomycin, polymyxin B, and dexamethasone:* *Ophthalmic dosage (drops):* 1–2 drops in the affected eye(s) 4–6 times a day. *Ophthalmic dosage (ointment):* A small amount (about ½ inch) in the affected eye(s) 3–4 times a day. *Neomycin, polymyxin B, and gramicidin:* *Ophthalmic dosage (eye drops):* 1–2 drops in the affected eye(s) every 4 hours for 7–10 days. For a more serious infection, dosage may be increased to as much as 2 drops per hour. *Neomycin, polymyxin B, and hydrocortisone:* *Ophthalmic suspension dosage:* 1–2 drops in the affected eye(s) every 3–4 hours.

TABLE 38.6 **Drug Emphasis Table: Ocular Antibacterials** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Ocular antibacterials can cause blurred vision; therefore, safety factors must be in place to prevent falls (uncluttered environment, adequate lighting, walking devices in reach). Hypersensitivity reactions to these drugs or any of their components can occur even with the first dose, so the nurse must make clients aware of this and tell them to seek treatment immediately. The drug should be discontinued at the first appearance of a skin rash.

Use of antibacterials over a prolonged period can deplete the normal flora, causing a superinfection. If this occurs, the treatment plan may need to be modified to add an antifungal agent. If the superinfection is bacterial, the overgrowth of this new organism may be resistant to the antibiotic's activity, and another appropriate antibacterial will need to be initiated.

Because they have a broad spectrum of activity against multiple organisms, ocular antibacterials are often overused, which can lead to the development of bacterial resistance. If purulent discharge, inflammation, or pain becomes worse, the client should discontinue the drug and contact a health care provider.

During the first 7 days of treating a corneal ulcer with ciprofloxacin drops, a nonharmful white crystalline precipitate commonly forms on the corneal defect. This precipitate will resolve on its own and causes no corneal damage

(DailyMed, *Ciprofloxacin*, 2022).

If ciprofloxacin is concurrently given with a systemic fluoroquinolone, arthropathy (tendon inflammation and tendon rupture) can occur. This usually occurs in young and older populations.

Table 38.7 is a drug prototype table for ocular antibacterials featuring ciprofloxacin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Ocular antibacterial **Mechanism of Action** Inhibits bacterial DNA synthesis	**Drug Dosage** *For bacterial conjunctivitis:* *Ophthalmic dosage (ointment):* ½-inch strip of ointment in the affected eye(s) 3 times a day for the first 2 days, then a ½-inch strip in the affected eye(s) 2 times a day for the next 5 days. *Ophthalmic dosage (solution):* 1–2 drops in the affected eye(s) every 2 hours, while awake, for 2 days. Then 1–2 drops in the affected eye(s) every 4 hours, while awake, for the next 5 days. *For corneal ulcers:* *Ophthalmic dosage (solution):* Day 1: 2 drops in the affected eye(s) every 15 minutes for the first 6 hours, and then 2 drops in the affected eye(s) every 30 minutes for the rest of the day, while awake. Day 2: 2 drops in the affected eye(s) every hour, while awake. Days 3–14: 2 drops in the affected eye(s) every 4 hours, while awake.
Indications Bacterial conjunctivitis Corneal ulcers **Therapeutic Effects** Bactericidal effects on a broad range of gram-negative and gram-positive organisms Decreased conjunctival redness and edema Reduced eye drainage and pain	**Drug Interactions** Systemic quinolones **Food Interactions** No significant interactions
Adverse Effects Eye burning or discomfort Foreign body sensation White precipitate on cornea Photophobia Blurred vision/decreased vision Hypersensitivity Superinfection	**Contraindications** Hypersensitivity to any of the ingredients in ciprofloxacin or any quinolone

TABLE 38.7 **Drug Prototype Table: Ciprofloxacin 0.3% Ophthalmic Solution** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ocular antibacterials:

- Consistently use aseptic techniques when giving the drug to prevent further infection (Iskandar et al., 2022).
- Teach the client the proper techniques for administering and storing the medication (Iskandar et al., 2022).
- Encourage the client not to wear contact lenses until treatment is completed and the bacteria eradicated.
- Evaluate for therapeutic effectiveness: decreased conjunctival erythema, drainage, and eye discomfort.
- Assess for hypersensitive reactions, such as hives, pruritus, facial/tongue/pharyngeal swelling, or difficulty

breathing.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ocular antibacterial should:

- Wash off any eye makeup and wash hands thoroughly prior to medication administration.
- Understand that they are still contagious until they have been receiving medication for 24–48 hours.
- Seek immediate attention if experiencing any hypersensitivity reactions such as severe eye redness or irritation of the eye, eyelids, lips, or face.
- Notify their health care provider if symptoms are not improving or are worsening.
- Protect eyes by wearing sunglasses when outside.

The client taking an ocular antibacterial *should not:*

- Drive or operate machinery with blurred vision.
- Wear contact lenses during the course of treatment.

Ocular Antivirals

Antiviral agents are used to treat herpes simplex ocular infections and primary keratoconjunctivitis. Trifluridine (Viroptic) is the most commonly administered antiviral ophthalmic drug. This is a locally active drug and is available in solution form. Systemic absorption is negligible, which reduces the risk of systemic adverse effects. This drug does not affect liver or kidney function. The overall action of this drug is to suppress viral replication. If there are no signs of improvement after 7 days of therapy or if there is incomplete re-epithelialization, continued use of this drug is not recommended and another therapy should be considered (DailyMed, *Trifluridine*, 2021).

Adverse Effects and Contraindications

Because this drug is locally acting, it causes very few adverse effects. Most of them are ocular-related. Continuous administration of trifluridine for periods exceeding 21 days should be avoided because of potential ocular toxicity. Rare adverse effects include keratitis sicca, hyperemia, epithelial keratopathy, and increased IOP. This drug is considered carcinogenic and can be extremely harmful if it enters the bloodstream; therefore, safety precautions such as handwashing and wearing gloves must be in place.

There are no true contraindications except for hypersensitivity to the drug's active and nonactive ingredients. If a client has a known sensitivity to any of the ingredients, the drug should be avoided (DailyMed, *Trifluridine*, 2021).

Table 38.8 is a drug prototype table for ocular antivirals featuring trifluridine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Ocular antiviral **Mechanism of Action** Interferes with DNA synthesis in cultured mammalian cells; antiviral mechanism of action is not completely known	**Drug Dosage** 1 drop on cornea of affected eye(s) every 2 hours while awake; maximum dose: 9 drops daily until corneal ulcer has completely re-epithelialized. *Following re-epithelialization:* 1 drop every 4 hours while awake for an additional 7 days; minimum daily dose: 5 drops.
Indications Primary keratoconjunctivitis Recurrent epithelial keratitis due to herpes simplex virus, types 1 and 2 **Therapeutic Effects** Inhibits viral replication by causing formation of defective viral proteins	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Mild, transient burning or stinging upon administration Palpebral conjunctival edema Ocular toxicity Retinal detachment	**Contraindications** Hypersensitivity to drug

TABLE 38.8 **Drug Prototype Table: Trifluridine 1% Ophthalmic Solution** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ocular antivirals:

- Dispose of the drug or container by adhering to the biohazard procedures of the facility.
- Refrigerate the solution at 36°F–48°F.
- Teach the client proper handling, administration, and disposal of the drug.
- Assess for a decrease in conjunctival erythema and potential adverse effects.
- Assess for manifestations of retinal detachment, such as floaters, flashes of light, or a shadow falling over their vision.
- Take precautions when caring for the client because viral infections are contagious.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ocular antiviral should:

- Immediately notify the health care provider if they experience reduced vision, floaters, flashes of light, or a curtain-like shadow over their field of vision because these could be signs of retinal detachment.
- Use the proper technique when administering and discarding any of the drug or container.
- Store the medication in the refrigerator to maintain its potency.
- Thoroughly wash face, hands, and any exposed skin after handling medication.
- Understand that viral infections are contagious and may remain so until they are completely gone.

The client taking an ocular antiviral *should not:*

- Instill the eye drops if they are not at room temperature because this can cause injury and pain.
- Assume that the organism has been fully eliminated because herpes lies dormant until something triggers it to become active.

Ocular Antifungals

Topical antifungals are active against a variety of yeast and filamentous fungi. Some of these include *candida*,

aspergillus, *cephalosporium*, *fusarium*, and *penicillium*. The only FDA-approved drug for ocular fungal infections is natamycin (Natacyn). This is a polyene antibiotic. Although the activity against fungi is dose-related, this drug is predominantly fungicidal. Because it is prepared in a suspension formula, it must be shaken well before using. Approximately 2% of this drug enters the body systemically, but this is an insufficient concentration to cause systemic issues. Most of the drug adheres to the cornea for desired periods of time without causing secondary damage. This drug does not enter intraocular fluid; therefore, it does not increase eye pressure. Continuation of therapy is determined by clinical picture and laboratory studies.

It may be helpful to decrease the dosage gradually at 4- to 7-day intervals to ensure the replicating organism has been eliminated. Failure to improve within 10 days indicates that the organism may not be related to a fungus. If true, the organism may be resistant to natamycin, and a different drug may be prescribed.

Adverse Effects and Contraindications

There are no true contraindications except for hypersensitivity to the drug's active and nonactive ingredients. If one has a known sensitivity to any of the ingredients, the drug should be avoided (DailyMed, *Natacyn*, 2023).

Table 38.9 is a drug prototype table for ocular antifungals featuring natamycin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Ocular antifungal **Mechanism of Action** Binds to sterols on the fungal cell membrane altering cell membrane permeability, causing leakage of essential intracellular contents	**Drug Dosage** 1 drop in the affected eye(s) every 1–2 hours for 3–4 days. Then 1 drop 6–8 times a day for 14–21 days.
Indications Fungal blepharitis, conjunctivitis, and keratitis caused by susceptible organisms **Therapeutic Effects** Inhibits reproduction of the organism (fungistatic) or kills the organism (fungicidal)	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Allergic reaction Change in vision Corneal opacity Chest pain Dyspnea Paresthesia Eye discomfort/irritation Conjunctival hyperemia Foreign body sensation Excess tearing (lacrimation)	**Contraindications** Hypersensitivity to drug

TABLE 38.9 **Drug Prototype Table: Natamycin 5% Ophthalmic Suspension** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking ocular antifungals:

- Shake the medication well so all the particles are evenly mixed.
- Be observant for any manifestations of hypersensitivity (e.g., skin rash, hives, eye pain, or swelling of the face, lips, or tongue), and provide treatment immediately (Cleveland Clinic, 2023b).
- Assess for therapeutic effects (e.g., decreased eye pain, redness, and tearing along with increased visual acuity).
- Be certain the medication is being correctly administered and no doses are missed, because fungal infections

are very difficult to treat.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ocular antifungal should:

- Notify the health care provider if experiencing hives, difficulty breathing, tunnel vision, chest pain, dyspnea, alteration in visual acuity, or paresthesia ("pins and needles" sensation) because these may represent adverse reactions.

The client taking an ocular antifungal *should not:*

- Use before the suspension has been adequately shaken and there is a uniform mixture.
- Wear contact lenses before treatment is completed. If this is not feasible, contact lenses can be inserted no earlier than 15 minutes after the drug has been administered.

38.3 Ocular Anesthetics and Lubricants

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 38.3.1 Identify the characteristics of ocular anesthetic and lubricant drugs used to treat eye disorders.
- 38.3.2 Explain the indications, actions, adverse reactions, and interactions of ocular anesthetic and lubricant drugs used to treat eye disorders.
- 38.3.3 Describe the nursing implications of ocular anesthetic and lubricant drugs used to treat eye disorders.
- 38.3.4 Explain the client education related to ocular anesthetic and lubricant drugs used to treat eye disorders.

Ocular Anesthetics

Local anesthesia blocks nerve conduction of sensory impulses and motor impulses from the periphery to the CNS. Sodium channels are blocked to inhibit increases in permeability of the nerve membrane required for an action potential. Because the initiation and propagation of action potentials is deterred, sensation cannot be transmitted from the source of stimulation to the brain.

Several ophthalmic procedures require adequate local anesthesia of the eyes. Some of these procedures include measurement of intraocular pressure, removal of foreign bodies, repairing corneal damage with sutures, Lasik surgery, conjunctival scraping, and gonioscopic examination to detect signs of glaucoma. Prolonged use of a topical ocular anesthetic may produce permanent corneal opacification with accompanying loss of vision (Sharifi et al., 2022).

CLINICAL TIP

Identifying Names of Local Anesthetics

All ocular anesthetic medications end in the suffix "caine." This is useful to know when the nurse does not recognize the drug's name but can identify it is an anesthetic based on its suffix.

Proparacaine HCL

Proparacaine is a topical anesthetic used prior to surgical operations such as cataract extraction. This drug has a rapid onset with a short duration; therefore, it is usually given in repeated doses. Also, clients should not touch the eye while it is numb to avoid accidental injury due to the insensitivity of the eye (Mayo Clinic, 2023b).

Tetracaine HCL

This drug has a slow onset with a long duration of action. It may only need to be administered once. Clients should

not touch the eye while it is numb to avoid accidental injury due to the insensitivity of the eye (Mayo Clinic, 2023b).

Table 38.10 lists common ocular anesthetics and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Proparacaine (Alcaine, Ocu-Caine)	*0.5% ophthalmic solution:* *For ophthalmic anesthesia:* 1–2 drops in affected eye(s) before the procedure. *For anesthesia in short corneal and conjunctival procedures:* 1 drop in affected eye(s) every 5–10 minutes for 5–7 doses.
Tetracaine (Pontocaine, Ametop)	*0.5% or 1% tetracaine hydrochloride solution:* 1–2 drops in eye(s) as needed. Doses vary depending on ophthalmic procedure: *Corneal foreign body or suture removal:* 1–2 drops in affected eye(s) every 5–10 minutes for 1–3 doses. *Brief ophthalmic anesthesia (tonometry or short corneal/conjunctival procedures):* 1–2 drops in eye(s) prior to starting the procedure. *Prolonged ophthalmic anesthesia (e.g., cataract extraction or other extended procedures):* 1–2 drops in affected eye(s) every 5–10 minutes for 3–5 doses.

TABLE 38.10 **Drug Emphasis Table: Ocular Anesthetics** (sources: https://dailymed.nlm.nih.gov/dailymed/; Stringer et al., 2023)

Adverse Effects and Contraindications

Local effects of stinging, burning, or redness can occur. Prolonged use or misuse can lead to corneal epithelial toxicity, resulting in opacity of the cornea with varying levels of vision loss. With the use of proparacaine, a rare, severe, immediate, apparently hyperallergic corneal reaction may occur, characterized by acute, intense, and diffuse epithelial keratitis; a gray, ground-glass appearance; sloughing of necrotic epithelium; corneal filaments (strands composed of degenerated epithelial cells and mucus that adhere to the cornea); and iritis (inflammation of the iris) with descemetitis (membrane inflammation) (DailyMed, *Proparacaine*, 2023).

Table 38.11 is a drug prototype table for ocular anesthetics featuring proparacaine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Ocular anesthetic **Mechanism of Action** Temporarily blocks sodium ion channels, which inhibits increases in permeability of the nerve membrane, thus preventing the initiation and conduction of action potentials, which prevents the transmission of sensation from the area being stimulated to the brain	**Drug Dosage** *0.5% ophthalmic solution:* *For ophthalmic anesthesia:* 1–2 drops in the affected eye(s) before the procedure. *For anesthesia in short corneal and conjunctival procedures:* 1 drop in the affected eye(s) every 5–10 minutes for 5–7 doses.
Indications For procedures in which a topical ophthalmic anesthetic is indicated **Therapeutic Effects** Promotes anesthesia (numbing)	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Transient stinging or burning Conjunctival erythema (redness) Ocular pain/discomfort Possible vision loss due to corneal opacity Diffuse epithelial keratitis	**Contraindications** Hypersensitivity to any of the ingredients

TABLE 38.11 **Drug Prototype Table: Proparacaine 0.5% Ophthalmic Solution** (sources: https://dailymed.nlm.nih.gov/dailymed/; Sharifi et al., 2022)

Nursing Implications

The nurse should do the following for clients who are taking ocular anesthetics:

- Conduct a thorough preoperative assessment including past experience with ocular surgery, cardiac and respiratory issues, pain tolerance, past medical history, allergies, and medication list, including use of anticoagulants.
- Perform postoperative assessment as prescribed. Be especially aware of pain level because this indicates the anesthesia is wearing off.
- Ensure there is adequate lighting and lack of clutter to promote client safety.
- Frequently remind clients not to touch their eyes while the eye is still numb to avoid ocular injuries.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ocular anesthetic should:

- Tell the health care provider about a history of falls, ambulation deficits, and the use of ambulatory aids. Ocular anesthetic drops can alter perception and potentially lead to a fall.
- Inform the health care provider if there is a progressive deterioration in vision.
- Let the nurse know if they are experiencing any ocular pain.

The client taking an ocular anesthetic *should not:*

- Touch their eyes while still numb from ocular anesthetics to avoid accidental injury due to insensitivity of the eye.
- Attempt to ambulate independently if vision is unclear.

Ocular Lubricants

Eye lubricants are used to temporarily relieve burning, irritation, and discomfort caused by dry eyes. They serve as a protector from further eye irritation. These products come in various forms: gel, ointment, emulsion, and solution. Most of these can be found over-the-counter (OTC); therefore, it is important clients follow the printed instructions. Some ophthalmic lubricants are antimicrobial and reduce the risk of infection. Others constrict blood vessels and reduce redness in the eye; still others contain zinc sulfate, an astringent that dries the mucus and relieves eye irritation.

Artificial tears and white petrolatum/mineral oil are more similar than different (Khan, n.d.). Artificial tears come in solution form. The active ingredients are glycerin and propylene glycol, which are clear isotonic solutions and should not be used if the color changes or the solution becomes cloudy. White petrolatum/mineral oil is available as an ointment. The active ingredients are mineral oil and white petrolatum.

Table 38.12 lists common ocular lubricants and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Artificial tears (LubriTears, Systane)	1–2 drops in affected eye(s) on an as-needed basis for dry or irritated eyes.
White petrolatum/mineral oil (Lacri-Lube)	¼ inch of ointment to inside of eyelid as needed.

TABLE 38.12 Drug Emphasis Table: Ocular Lubricants (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

The adverse effects of ocular lubricants include ocular burning, itchy watery eyes, blurred vision, and sensitivity to light (Drugs.com, 2023).

Table 38.13 is a drug prototype table for ocular lubricants featuring white petrolatum/mineral oil. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and

contraindications.

Drug Class Ocular lubricant **Mechanism of Action** Reduces the osmolarity of the tear film and/or dilutes inflammatory substances	**Drug Dosage** ¼ inch of ointment to inside of eyelid as needed.
Indications For the temporary relief of burning, irritation, and discomfort due to dryness of the eye or exposure to wind or sun As a protectant against further irritation **Therapeutic Effects** Replaces missing tear constituents for relief of burning and irritation	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Blurred vision Stickiness of eyelashes from ointment Stinging Eye pain Eye redness	**Contraindications** Allergy to any inactive ingredient

TABLE 38.13 **Drug Prototype Table: White Petrolatum/Mineral Oil** (sources: https://dailymed.nlm.nih.gov/dailymed/; Drugs.com, 2023)

Nursing Implications

The nurse should do the following for clients who are taking ocular lubricants:

- For the client who is intubated and is not spontaneously blinking, who is unconscious, or who is unable to close their eyes and blink, the nurse must assess the eye frequently and use a damp cloth to remove prior lubricant to avoid buildup or crusting.
- Observe the client's entire face and cleanse the areas around the eyes and face to promote hygiene and avoid infection.
- Evaluate therapeutic effectiveness of medication and observe for hypersensitivity reactions such as rash, dizziness, difficulty breathing, or itching or swelling of the face, tongue, or throat.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an ocular lubricant should:

- Be careful not to contaminate the tip of the dispenser because this may cause an eye infection.
- Notify the health care provider if symptoms are not improving or are getting worse.
- Use appropriate technique when instilling the lubricant.

The client taking an ocular lubricant *should not:*

- Continue using the medication if they experience eye pain, vision changes, continued redness, or irritation of the eyes.
- Double the dose if they missed one (Cleveland Clinic, 2023a).
- Drive or engage in hazardous activity until vision has cleared.

38.4 Antiglaucoma Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 38.4.1 Identify the characteristics of antiglaucoma drugs used to treat glaucoma-related eye disorders.
- 38.4.2 Explain the indications, actions, adverse reactions, and interactions of antiglaucoma drugs used to treat glaucoma-related eye disorders.
- 38.4.3 Describe the nursing implications of antiglaucoma drugs used to treat glaucoma-related eye disorders.
- 38.4.4 Explain the client education related to antiglaucoma drugs used to treat glaucoma-related eye disorders.

There are two common forms of glaucoma: primary open-angle glaucoma (POAG), which is the most common form, and acute angle-closure (narrow-angle) glaucoma. These differ with respect to underlying pathology and treatment. Treatment of POAG focuses on reducing elevated IOP, the only risk factor that can be modified. Although no cure exists, reducing IOP can slow or even cease disease progression. Drugs lower IOP by either promoting aqueous humor drainage or reducing the production of aqueous humor. First-line drugs belong to three classes: beta-adrenergic blockers (beta blockers), alpha-2 adrenergic agonists, and prostaglandin analogs. Carbonic anhydrase inhibitors are considered second-line drugs. All of these medications are available in ophthalmic form, which is the preferred route. Because these classifications lower IOP by different mechanisms, combined therapy is usually more effective than monotherapy. If sufficient amounts of drug enter the circulation, systemic adverse effects may occur (Farkouh et al., 2016).

Angle-closure glaucoma is triggered by displacement of the iris where it covers the trabecular meshwork. The angle between the cornea and the iris is greatly reduced. This prevents aqueous humor from leaving the anterior chamber. IOP levels increase rapidly to dangerous levels. The client will complain of severe ocular pain and headache. Permanent vision loss may occur within 24–48 hours if left untreated. Treatment consists of a combination of drugs to suppress symptoms. Once the IOP is reduced to a safe level, the client will undergo surgery on the iris. This is performed to allow unobstructed outflow of aqueous humor.

Nonadherence is an issue for POAG drugs for multiple reasons. These include the asymptomatic nature of the condition such that clients may feel drug therapy is unnecessary, frequent dosing intervals, multiple drugs to administer, and age-related issues (see the box below). It is essential to emphasize to the client the importance of having regular eye exams to track progress or identify complications (Centers for Disease Control and Prevention, 2020).

SPECIAL CONSIDERATIONS

Older Adults

Glaucoma affects older adults more than any other population. Due to the complexity of treatment, older adults may struggle with following the treatment plan. This occurs for various reasons including:

- Forgetfulness due to mild cognitive impairment (MCI) or dementia
- Inability to remember in which sequence to administer the multiple drugs
- High cost
- Inability to properly instill eye medication
- Medication causing temporary blurry vision, leading to an increased risk for falls

Concerns related to specific drug classifications include:

- Beta blockers may exacerbate heart failure in those who have a history of this condition.
- Alpha-2 agonists can cause orthostatic hypotension, creating a risk for falls.
- Those with inadequate renal function should avoid carbonic anhydrase inhibitors.

Beta-Adrenergic Blockers

Beta blockers reduce IOP by decreasing the production of aqueous humor. They are mainly used to treat

POAG. These drugs are suitable for both initial and maintenance therapy. Beta blockers, in conjunction with other drugs, are also used for emergency management of acute narrow-angle glaucoma. Some ophthalmic beta blockers can be absorbed in sufficient amounts to create systemic adverse effects, including angina, upper respiratory infection, and muscle or joint pain (Haga et al., 2022); therefore, health care personnel and clients should be aware of these. This classification of drugs does not cause miosis like other classes and must be used in combination for angle-closure glaucoma.

In some clients, the lowering of intraocular pressure may require a few weeks to stabilize. More information on systemic administration of this classification can be found in Antihypertensive and Antianginal Drugs.

Betaxolol Hydrochloride (Cardioselective)

Betaxolol is a selective blocker for the beta-1 adrenergic receptors. The onset of this drug generally occurs within 30 minutes, and peak effect is reached in about 2 hours after administration. A single dose has a duration of 12 hours. Studies have shown clients treated with this drug for up to 3 years have maintained lowered IOP levels (DailyMed, *Betaxolol*, 2023).

Timolol Hydrochloride (Nonselective)

The onset of timolol is 30 minutes. Peak effects occur in 1–2 hours, and the duration of action is 24 hours. This allows the drug to be given once daily. Clients studied over a period of 1 year exhibited well-maintained IOP levels (DailyMed, *Timolol*, 2023).

CLINICAL TIP

Identifying Names of Beta Blockers

All beta blockers end in the suffix "olol." This is useful to know when the nurse does not recognize the drug's name but can identify it is a beta blocker based on its suffix.

Table 38.14 lists common beta-adrenergic blockers and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Betaxolol hydrochloride (Betoptic)	*Ophthalmic dosage (0.25% suspension):* 1 drop in affected eye(s) twice daily; maximum dose: 2 drops/day. *Ophthalmic dosage (0.5% solution):* 1–2 drops in affected eye(s) twice daily; maximum dose: 4 drops/day.
Carteolol hydrochloride (Ocupress)	1 drop 1% solution applied to conjunctiva of affected eye(s) twice daily; maximum dose: 2 drops/day.
Timolol hydrochloride (Timoptic)	*Ophthalmic dosage (solution):* 1 drop of 0.25% solution in affected eye(s) twice daily; may increase to 1 drop of 0.5% solution twice daily, if necessary for adequate reduction of intraocular pressure. Dosage may be reduced to 1 drop daily if effective to maintain reduced pressure. *Ophthalmic dosage (Timoptic-XE gel):* 1 drop of 0.25% solution in affected eye(s) once daily; may increase to 1 drop of 0.5% solution once daily, if necessary for adequate reduction of intraocular pressure. Doses greater than 1 drop of the 0.5% solution once daily have not been studied.

TABLE 38.14 **Drug Emphasis Table: Beta-Adrenergic Blockers** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Ocular beta-adrenergic blockers are contraindicated in clients who have a known hypersensitivity to any of the ingredients. They also are contraindicated in clients with sinus bradycardia, second- or third-degree AV block, cardiogenic shock, or severe heart failure.

Ocular adverse effects of beta-adrenergic blockers include eye pain, itching or discomfort, corneal sensitivity, eye erythema, keratitis, and photophobia. Although there is less concern about systemic effects when using beta blockers topically, some systemic absorption can occur when direct pressure is not applied to the medial canthus to

occlude the nasolacrimal sac. If adequate amounts of drug reach the circulation, the client may experience some systemic adverse effects. These effects may include bradycardia, hypotension, heart block, or worsening of heart failure. Dyspnea and bronchospasm can occur in clients with severe respiratory conditions like chronic obstructive pulmonary diseases (COPD) and asthma who are taking a nonselective beta blocker (timolol) but are less likely to occur with cardioselective agents (betaxolol). Additionally, CNS effects including dizziness, vertigo, lethargy, and headaches have been associated with the use of beta blockers. Because of the potential effect on heart rate, beta blockers may mask the symptoms of hypoglycemia in clients with diabetes (DailyMed, *Timolol*, 2023).

Table 38.15 is a drug prototype table for beta-adrenergic blockers featuring timolol. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications

Drug Class Beta-adrenergic blocker **Mechanism of Action** Reduces the production of aqueous humor by blocking the sympathetic nerve endings in the ciliary process	**Drug Dosage** *Ophthalmic dosage (solution):* 1 drop of 0.25% solution in affected eye(s) twice daily; may increase to 1 drop of 0.5% solution twice daily, if necessary for adequate reduction of intraocular pressure. Dosage may be reduced to 1 drop daily if effective to maintain reduced pressure. *Ophthalmic dosage (Timoptic-XE gel):* 1 drop of 0.25% solution in affected eye(s) once daily; may increase to 1 drop of 0.5% solution once daily, if necessary for adequate reduction of intraocular pressure. Doses greater than 1 drop of the 0.5% solution once daily have not been studied.
Indications Primary open-angle glaucoma Ocular hypertension **Therapeutic Effects** Decreases the amount of aqueous humor in the anterior chamber	**Drug Interactions** Other antihypertensives **Food Interactions** No significant interactions
Adverse Effects Transient ocular stinging Bradycardia Second- or third-degree heart block Hypotension Bronchospasm	**Contraindications** Sinus bradycardia Atrioventricular block Heart failure Cardiogenic shock COPD Asthma Caution: Diabetes mellitus (due to masking symptoms of hypoglycemia) COPD Asthma

TABLE 38.15 **Drug Prototype Table: Timolol** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking beta-adrenergic blockers:

- Review the client's cardiovascular and respiratory history.
- Obtain information about the client's smoking and alcohol use.
- Monitor the client's heart rate and rhythm.
- Periodically assess blood pressure.
- Assess respiratory status, such as respiratory rate, lung sounds, and difficulty breathing.

- Monitor for signs of hypoglycemia in clients with diabetes.
- Emphasize the importance of holding pressure against the lacrimal sac at the medial canthus when administering.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a beta-adrenergic blocker should:

- Notify their provider if they are pregnant or planning to become pregnant.
- Notify the health care provider if dizziness, shortness of breath, wheezing, excess fatigue, peripheral edema, or palpitations occur.
- Be certain they occlude the inner canthus to avoid systemic absorption.
- Identify signs/symptoms of hypoglycemia and monitor blood glucose levels if they have diabetes because these drugs may mask hypoglycemia.

The client taking a beta-adrenergic blocker *should not:*

- Change positions quickly to avoid falls (especially older adults) because this may cause dizziness, which may result in a fall.
- Wear contact lenses during administration and for 15 minutes afterward.
- Operate machinery if feeling dizzy or lightheaded.

Carbonic Anhydrase Inhibitors

This classification of drugs reduces IOP by decreasing production of aqueous humor. They are not as effective as others; however, they are very beneficial when used as an adjunct therapy with other drug classes. Carbonic anhydrase is an enzyme found in many tissues of the body, including the eye. It speeds up the reaction of hydrating carbon dioxide and dehydrating carbonic acid.

During chronic use, dorzolamide accumulates in red blood cells (RBCs) as it binds to carbonic anhydrase. When the drug is stopped, it will wash out of the RBCs (DailyMed, *Dorzolamide*, 2021). Brinzolamide and dorzolamide have the same effects. A combination drug consisting of dorzolamide and timolol exists. The combination provides an additive effect for decreasing the production of aqueous humor. The therapeutic and adverse effects of timolol are discussed in a previous section of this chapter.

Table 38.16 lists common carbonic anhydrase inhibitors and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Brinzolamide 1% solution (Azopt)	1 drop, 3 times daily.
Dorzolamide 2% solution (Trusopt)	1 drop, 3 times daily when used alone. 1 drop, twice daily if used in combination with other topical glaucoma treatment.

TABLE 38.16 Drug Emphasis Table: Carbonic Anhydrase Inhibitors (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Clients with sulfonamide hypersensitivity can experience severe or even fatal reactions, such as Stevens–Johnson syndrome, toxic epidermal necrolysis, hepatic necrosis, aplastic anemia, or agranulocytosis. Sensitivity can occur regardless of the route of administration. If there are any signs of an allergic reaction, the client should notify the provider immediately. Local ocular adverse effects occur with chronic administration (DailyMed, *Brinzolamide*, 2023). Although acid–base imbalance and electrolyte disturbances primarily occur with the oral form, the potential should be considered with clients receiving this classification via the topical route. The risk of metabolic acidosis is compounded with concurrent use of high-dose salicylic acid. These adverse effects do disappear once the underlying condition is treated (Tang et al., 2023). Other adverse effects include alopecia, chest pain, conjunctivitis, diarrhea, diplopia (double vision), dizziness, dry mouth, dyspnea, dyspepsia, eye fatigue, hypertonia,

keratoconjunctivitis, keratopathy, kidney pain, lid margin crusting or a sticky sensation, nausea, pharyngitis, tearing, and urticaria (DailyMed, *Dorzolamide*, 2021).

Table 38.17 is a drug prototype table for carbonic anhydrase inhibitors featuring dorzolamide. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Carbonic anhydrase inhibitor **Mechanism of Action** Reduces the production of aqueous humor from the ciliary process by slowing the formation of bicarbonate ions with subsequent reduction in sodium and fluid transport	**Drug Dosage** 1 drop, 3 times daily when used alone. 1 drop, twice daily if used in combination with other topical glaucoma treatment.
Indications Primary open-angle glaucoma Ocular hypertension **Therapeutic Effects** Decreases the level of IOP	**Drug Interactions** High-dose salicylates Oral carbonic anhydrase inhibitors **Food Interactions** No significant interactions
Adverse Effects Ocular burning and stinging Bitter taste Superficial punctate keratitis Ocular allergic reaction (conjunctivitis, eyelid edema) Eye redness, photophobia, tearing Metabolic acidosis/hyperkalemia	**Contraindications** Allergy to sulfonamides Hypersensitivity to any component of this product

TABLE 38.17 **Drug Prototype Table: Dorzolamide** (sources: https://dailymed.nlm.nih.gov/dailymed/; Hoffmanova & Sanchez, 2018)

Nursing Implications

The nurse should do the following for clients who are taking carbonic anhydrase inhibitors:

- Monitor potassium levels periodically in clients with impaired renal function.
- Assess for signs/symptoms of metabolic acidosis, such as rapid breathing in clients with impaired renal function.
- Teach the client that they may experience a bitter taste and that this is not harmful.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a carbonic anhydrase inhibitor should:

- Be acclimated to the medication before operating machinery because they may experience fatigue, tiredness, or dizziness.
- Be aware that they may experience a bitter taste, stinging, burning, or conjunctival irritation.
- Stop taking the drug and contact their health care provider if they develop conjunctivitis or eyelid edema.
- Contact the health care provider immediately with any manifestations of ocular or systemic allergic reactions, such as skin rash, jaundice, right upper quadrant (RUQ) pain, or easy bruising (Mayo Clinic, 2023a).

The client taking a carbonic anhydrase inhibitor *should not:*

- Wear contact lenses during administration and for 15 minutes afterward because the preservative in the

medication will bind to the contacts.

Prostaglandin Analogues

These drugs are as effective as beta blockers without the serious adverse effects. The recommended daily dosage produces the same reduction in IOP as does twice-daily timolol. Prostaglandin analogues are considered first-line agents for glaucoma, especially in clients with cardiac conditions. In contrast to beta blockers, these drugs lower IOP by relaxing the ciliary muscle to facilitate aqueous humor outflow. If the drug is given more frequently or at a higher dose, this action can have the opposite effect and decrease the IOP-lowering effect (DailyMed, *Latanoprost*, 2023).

Latanoprost

The onset of action for latanoprost occurs in about 3–4 hours, and peak effect is reached in 8–12 hours. This drug has a 24-hour duration of action (DailyMed, *Latanoprost*, 2023).

Bimatoprost

The actions and adverse effects of bimatoprost are the same as those of latanoprost. When marketed as Latisse, it is used for the specific purpose of increasing eyelash length, darkening lashes, and making the lashes thicker (DailyMed, *Bimatoprost*, 2022).

Travoprost

The actions and adverse effects of travoprost are the same as those of latanoprost. This drug was found to be more effective in Black clients than in other groups. The reason for this is unknown (DailyMed, *Travoprost*, 2020).

CLINICAL TIP

Identifying Names of Prostaglandin Analogues

All prostaglandin analogues end in the suffix "prost." This is useful to know when the nurse does not recognize the drug's name but can identify it is a prostaglandin analogue based on its suffix.

Table 38.18 lists common prostaglandin analogues and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Latanaprost 0.005% solution (Xalatan)	1 drop in the affected eye(s) once daily in the evening.
Bimatoprost 0.01% and 0.03% solution (Lumigan)	1 drop in the affected eye(s) once daily in the evening.
Travoprost 0.004% solution (Travatan)	1 drop in the affected eye(s) once daily in the evening; maximum dose: 1 drop per day per affected eye.

TABLE 38.18 Drug Emphasis Table: Prostaglandin Analogues (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

On rare occasions and for reasons unknown, this drug classification can cause migraines. The most common adverse effect is ocular hyperemia, which is engorgement of ocular blood vessels.

There are two main contraindications: hypersensitivity and active intraocular inflammation. Clients with iritis or uveitis should not use this drug because the inflammation may worsen, which could have negative effects on vision (DailyMed, *Latanoprost*, 2023)

Table 38.19 is a drug prototype table for prostaglandin analogues featuring latanoprost. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Prostaglandin analogue **Mechanism of Action** Reduces IOP by increasing the outflow of aqueous humor through relaxation of the ciliary process and increasing the outflow at both the uveoscleral and trabecular meshwork structures	**Drug Dosage** 1 drop in the affected eye(s) once daily in the evening.
Indications Primary open-angle glaucoma Ocular hypertension Treatment of hypotrichosis of the eyelashes **Therapeutic Effects** Reduces the amount of IOP	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Ocular hyperemia Intraocular inflammation (iritis/uveitis) Foreign body sensation Local irritation, stinging Redness Blurred vision Heightened brown pigmentation of the iris Increased pigmentation of the eyelid Increased length and thickness of the eyelashes Burning or stinging Punctate keratopathy	**Contraindications** Hypersensitivity to the active and inactive ingredients of the drug Active intraocular inflammation Caution: Herpetic and bacterial keratitis

TABLE 38.19 **Drug Prototype Table: Latanoprost 0.005% Ophthalmic Solution** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking prostaglandin analogues:

- Assess for ocular changes, including hyperemia, pruritus, conjunctivitis, and visual disturbances.
- Explain the hyperpigmentation changes that can occur so the client is not alarmed. Be certain the client is aware that the hyperpigmentation of the iris is usually permanent, but the darkened skin of the eyelids more than likely will resolve.
- Assess for hypersensitivity reactions, both locally and systemically, including stinging, painful eyes and blurry vision.
- Explain that the medication should be administered at bedtime.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a prostaglandin analogue should:

- Notify the health care provider of ocular redness, swelling, or visual changes.
- Administer the medication at bedtime as ocular pressure is typically highest in the morning, so usage at night is a timely intervention to address an expected higher ocular pressure by morning.
- Observe for the hyperpigmentation changes and increase in eyelash length.

The client taking a prostaglandin analogue *should not:*

- Wear contact lenses during administration and for 15 minutes afterward because the preservative in the

medication will bind to the contacts.
- Skip follow-up appointments with the ophthalmologist for intraocular pressure measurements.

Rho Kinase Inhibitors

This drug class was approved in 2017. It decreases IOP by increasing aqueous humor outflow through the trabecular meshwork. The exact mechanism is unknown. Clinical trials have shown up to a 5 mm Hg reduction in the baseline IOP (DailyMed, *Rhopressa*, 2023).

The 0.02% solution of netarsudil (Rhopressa) is used to reduce IOP in clients with POAG. This drug is typically taken in the evening because IOP is elevated in the morning. The solution should not be administered while wearing contact lenses.

Adverse Effects and Contraindications

Conjunctival hyperemia is the most common ocular adverse effect. Clients may experience discomfort and erythema in the early phase of treatment; however, these will subside as the drug is continued. Corneal verticillata (gray-brown opacities) were noted to develop at 4 weeks of therapy. This reaction did not affect visual acuity. Most corneal verticillata will disappear once the medication is discontinued. Besides the physical aspect, conjunctival hemorrhage is harmless and will resolve on its own. Other common adverse reactions include conjunctival hemorrhage, corneal staining, blurred vision, increased lacrimation, and reduced visual acuity. Safety and effectiveness in clients under age 18 have not been established. Hypersensitivity is currently the only major contraindication (DailyMed, *Rhopressa*, 2023).

Table 38.20 is a drug prototype table for rho kinase inhibitors featuring netarsudil. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Rho kinase inhibitor 0.02% solution **Mechanism of Action** Inhibits the rho kinase enzyme, thus reducing IOP by increasing the outflow of aqueous humor through the trabecular meshwork	**Drug Dosage** 1 drop of solution in the affected eye(s) every evening.
Indications Primary open-angle glaucoma Ocular hypertension **Therapeutic Effects** Reduces elevated IOP Increased healing of corneal epithelium Decreases progression of diabetic retinopathy	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Conjunctival hyperemia Eye discomfort and/or erythema during instillation Conjunctival hemorrhage Corneal verticillata Increased lacrimation Reduced visual acuity	**Contraindications** None

TABLE 38.20 **Drug Prototype Table: Netarsudil 0.02% Ophthalmic Solution** (sources: https://dailymed.nlm.nih.gov/dailymed/; Moshirfar et al., 2018)

Nursing Implications

The nurse should do the following for clients who are taking rho kinase inhibitors:

- Inform the client they may experience discomfort and redness upon instillation during the initial treatment

phase, but this will subside.
- Encourage the client not to discontinue medication based on the adverse effects without contacting the health care provider.
- Maintain a safe environment to prevent falls.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a rho kinase inhibitor should:

- Notify the health care provider of eye swelling or changes in vision or if they experience conjunctivitis or eyelid discomfort.
- Understand the eye changes are mainly harmless and will subside spontaneously or once the drug is stopped.

The client taking a rho kinase inhibitor *should not:*

- Double up on a dose if one is missed because this is not well tolerated.
- Wear contact lenses during administration and for 15 minutes afterward because the preservative in the medication will bind to the contacts.
- Stop taking the drug without contacting the health care provider.

Alpha-2 Adrenergic Agonists

Alpha-2 adrenergic agonists work by reducing aqueous outflow to lower pressure. Combigan is an alpha-2 adrenergic agonist combined with a beta blocker (timolol). This drug synergistically uses both mechanisms of action to reduce IOP. If an ocular beta blocker is contraindicated, an alpha-2 adrenergic agent can be used alone. Brimonidine (Alphagan P) has a rapid onset of action with a half-life of 2 hours. Brimonidine reduces aqueous humor production and increases uveoscleral outflow in clients with POAG and ocular hypertension. It may have properties in delaying optic nerve degeneration and may protect retinal neurons from dying due to ischemia.

A fixed-dose combination drug consisting of brimonidine and timolol exists. The combination provides an additive effect for decreasing the production of aqueous humor. The therapeutic and adverse effects of each drug class are discussed previously in this chapter.

Adverse Effects and Contraindications

Brimonidine is contraindicated in those under age 2 because they are at a higher risk of CNS depression. Severe cardiovascular disease and vascular and cerebral insufficiency can be aggravated by this drug classification (DailyMed, *Brimonidine,* 2023). There has been a causal relationship noted between depression and alpha-2 agonists. Because the alpha-2 adrenergic receptors are part of the CNS, dilation of the pupils can occur, which will further impede the outflow of aqueous humor and exaggerate closed-angle glaucoma.

Table 38.21 is a drug prototype table for alpha-2 adrenergic agonists featuring brimonidine. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Alpha-2 adrenergic agonist **Mechanism of Action** Reduces production of aqueous humor and increases uveoscleral outflow	**Drug Dosage** 1 drop in the affected eye(s) every 8 hours of 0.1% or 0.15% solution.
Indications For lowering IOP in clients with open-angle glaucoma or ocular hypertension **Therapeutic Effects** Decreases pressure in the anterior chamber of the eye	**Drug Interactions** Monoamine oxidase (MAO) inhibitors Selective serotonin reuptake inhibitors (SSRIs) CNS depressants Antihypertensives/cardiac glycosides **Food Interactions** No significant interactions
Adverse Effects Ocular hypotension Systemic hypotension Tachycardia/bradycardia Fatigue Headache/dizziness Reduced attention span and alertness CNS depression Cough/dyspnea Sinusitis/nasal dryness Blepharitis Conjunctival edema/hemorrhage Eye dryness/irritation Allergic conjunctivitis/hyperemia/pruritus	**Contraindications** <2 years of age Hypersensitivity to the active and inactive ingredients of the drug Caution: Vascular insufficiency Advanced cardiac disease Cerebral insufficiency Raynaud's disease Thromboangiitis obliterans (Buerger's disease, where blood vessels are occluded in the hands and feet) Depression

TABLE 38.21 **Drug Prototype Table: Brimonidine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking alpha-2 adrenergic agonists:

- Review the client's past medical history and medications.
- Monitor the client's blood pressure and heart rate periodically.
- Assess the client's mental status and alertness.
- Maintain a safe environment and reduce risk of falls.
- Evaluate the upper respiratory system for cough, sinus pressure, dyspnea, and nasal dryness.
- Check for hypersensitivity reaction.
- Emphasize to the client the importance of keeping follow-up appointments with their health care provider.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an alpha-2 adrenergic agonist should:

- Notify the health care provider of severe headaches, visual disturbance, dizziness, syncope, excessive fatigue, difficulty concentrating, or vision changes.
- Check their blood pressure and heart rate at least weekly while maintaining a log of readings.

The client taking an alpha-2 adrenergic agonist *should not:*

- Wear contact lenses during administration and for 15 minutes afterward because the preservative in the

medication will bind to the contacts.
- Drive or engage in activity that requires attention and concentration until they know how the medications affects them.
- Get up quickly and ambulate because the drug can cause orthostatic hypotension and dizziness.

Chapter Summary

This chapter introduced various ophthalmic medications used for multiple purposes. Drugs were discussed based on their classification and primary mechanism of action. The eye itself can have ocular pathology, such as infection. Because the eye can be a portal of infection, it is essential that the nurse administer ocular medications via aseptic technique. In addition, the eye can also reflect illness, injury, and autoimmune systemic diseases. Ocular medications are available in several forms, including drops, solutions, gels, and ointments. Medications covered in this chapter included ocular anti-inflammatories, anti-infectives (antibacterials, antivirals, antifungals), anesthetics, lubricants, and drugs used to treat or manage glaucoma. The two main types of glaucoma were discussed, including the more common presentation of POAG as well as closed-angle glaucoma, which has a much quicker onset and can present as blindness.

Key Terms

accommodation ability of the lens to change shape when looking alternatively at a near object and far object

aqueous humor fluid typically produced in the posterior chamber of the eye, which nourishes the internal structures and maintains a homeostatic eye pressure

astigmatism when the cornea or lens is curved more steeply in one direction, causing light to focus on multiple points of the retina

canaloplasty eye surgery that uses a microcatheter to cannulate Schlemm's canal in order to restore aqueous humor outflow to lower intraocular pressure

cataracts cloudy areas on the lens of the eye from the breakdown of proteins that affect vision

cones receptors on the retina for daytime and color vision

conjunctival hyperemia excess of blood in the eye's vessels, causing redness

conjunctivitis infection and inflammation of the conjunctiva, causing redness and irritation; also referred to as "pink eye"

external ocular structures structures outside the eye responsible for protecting the eye and allowing the eye to rotate and move up and down

glaucoma group of diseases caused by obstruction or excess production of aqueous humor, resulting in loss of peripheral vision

hyperopia a condition in which light refracts behind the retina, resulting in close objects appearing blurry and far objects being clearly seen; also known as farsightedness

internal ocular structures structures inside the eye responsible for light accommodation, eye color, fluid to support eye pressure homeostasis, and the optic nerve

macular degeneration degeneration of the central portion of the retina, causing gradual loss of central vision

myopia a condition in which light refracts in front of the retina, resulting in far objects appearing blurry and near objects being clearly seen; also known as nearsightedness

photophobia abnormal sensitivity to light

presbyopia a condition that occurs as one ages; the lens thickens and becomes less elastic, which makes it difficult for the eyes to accommodate

refractive errors when light does not shine directly on the retina, causing distorted vision

rods receptors on the retina for nighttime vison

trabeculectomy eye surgery that creates a bypass of obstructed aqueous fluid in the trabecular network to prevent further loss of vision in glaucoma

Review Questions

1. Which teaching point should the nurse include when educating clients about the administration of trifluridine?
   a. "Wear gloves when handling and instilling this medication."
   b. "This drug is absorbed into the body and causes many adverse effects."
   c. "Instill the medication by pulling the upper lid toward the forehead."
   d. "This drug is effective against both bacterial and viral infections."

2. Which medication should the nurse anticipate being prescribed to prevent ophthalmia neonatorum due to *Neisseria gonorrhea*?
   a. Tetracaine
   b. Erythromycin

c. Timolol
d. Latanoprost

3. A client states that they have been told they are a "glaucoma suspect." The nurse understands this means the client has one or more risk factors from which of the following groups?
a. Elevated intraocular pressure, optic nerve damage, visual field deficits
b. Elevated intraocular pressure, decreased cornea thickness, optic nerve damage
c. Decreased intraocular pressure, strong family history of glaucoma, optic nerve atrophy
d. Decreased intraocular pressure, increased cornea thickness, optic nerve damage

4. Which complication of untreated "pink eye" should the nurse teach to a parent of a child with eye redness and a thick discharge?
a. Diplopia
b. Macular degeneration
c. Glaucoma
d. Meningitis

5. During an intake history, a client tells the nurse that they are taking an eye drop that changed the color of their eyelids and caused their eyelashes to thicken and grow, but they cannot remember the name of the drug. Which ophthalmic drug class should the nurse anticipate the client is taking?
a. Beta blockers
b. Carbonic anhydrase inhibitors
c. Prostaglandin analogues
d. Alpha-2 adrenergic agonists

6. Which prostaglandin analogue does the nurse understand to be more effective in Black clients?
a. Latanoprost
b. Travoprost
c. Brimonidine
d. Netarsudil

7. A client tells the clinic nurse that after administering timolol drops in their right eye, they noticed that their heart rate decreased to 50 beats per minute. Which question by the nurse best determines the most likely cause of bradycardia?
a. "Did you drink alcohol that day?"
b. "Have you had heart trouble before?"
c. "How did you take your pulse?"
d. "How did you instill the medication?"

8. A client is taking prednisolone drops for uveitis. Which condition that can occur with prolonged use should the nurse warn the client about?
a. Blepharitis
b. Conjunctivitis
c. Chalazion
d. Cataracts

9. A client has been prescribed an ocular antiviral, trifluridine, for ocular herpes. The nurse instructs the client to seek immediate treatment if they experience which condition?
a. Floaters and flashes of light
b. Fatigue
c. Hordeolum
d. Tearing of the eye

10. Which potential systemic effect should the nurse anticipate when administering a nonselective ophthalmic beta blocker?

a. It may mask signs of hypoglycemia.
b. It may decrease peripheral edema.
c. It may reduce bronchospasm.
d. It may increase heart rate.

CHAPTER 39
Otic Drugs

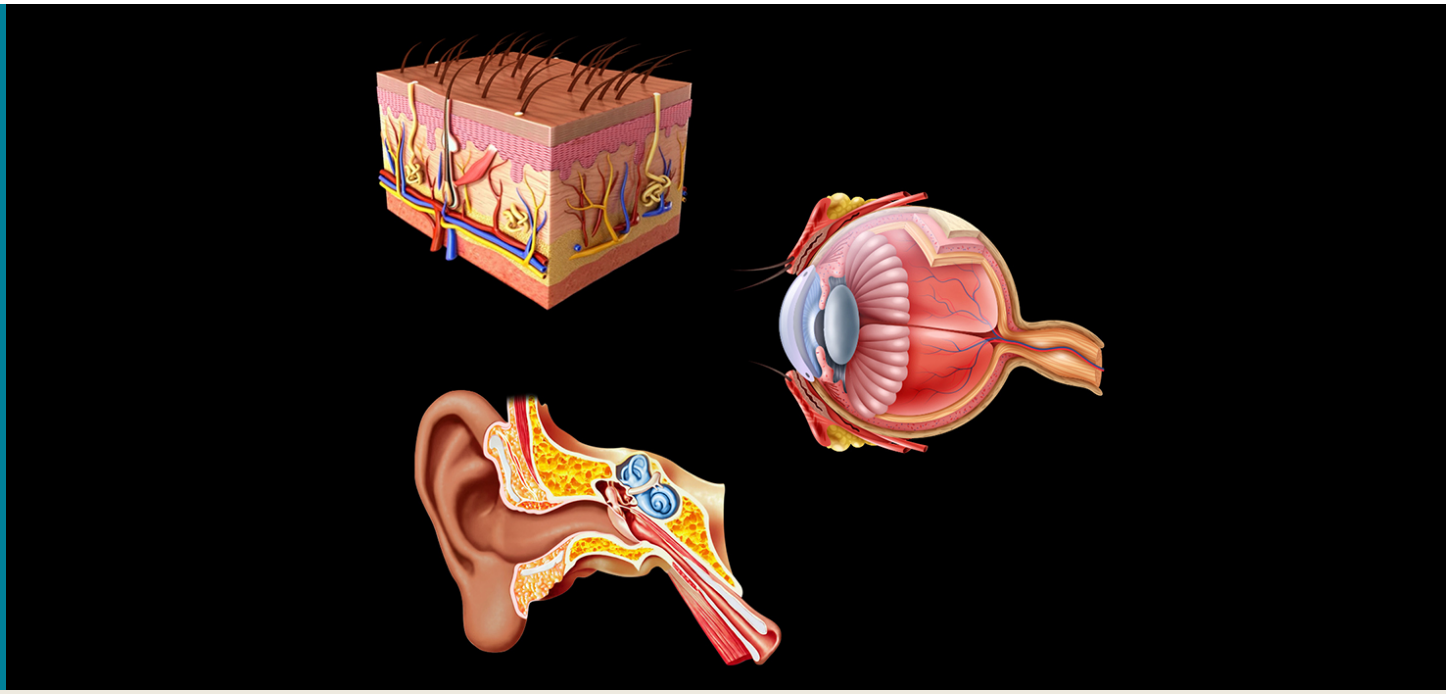


FIGURE 39.1 Maintaining clients' health can include understanding pharmacological options that enhance vision, auditory health, and skin wellness. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The human ear is composed of multiple structures that aid in providing balance, spatial sensation, and hearing. The ear is an extension of the central nervous system. Cognition can be compromised when sound is not effectively transmitted. This chapter will address the structure and function of the ear, common ear disorders, and otic medications.

39.1 Introduction to the Ears

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 39.1.1 Describe the structures and functions of the ears.
- 39.1.2 Identify common types of ear disorders.

Ear Structure and Function

The ear is connected to the central nervous system through inputs from the **vestibulocochlear nerve**—the eighth cranial nerve—which transmits sound from the inner ear to the auditory cortex in the temporal lobe of the brain. The vestibulocochlear nerve splits into the vestibular and cochlear nerves. The **vestibular nerve** controls motion and position; the **cochlear nerve** transmits signals from the cochlea to the temporal lobe in the brain so that sound can be heard. Sensorineural hearing loss (SNHL) is the most common type of hearing loss and accounts for the majority of all hearing loss. SNHL refers to any cause of hearing loss due to a pathology of the cochlea, auditory nerve, or central nervous system (Tanna et al., 2023).

The external ear, the middle ear, and the inner ear comprise the ear, as shown in Figure 39.2. The external ear—also called the outer ear, pinna, or auricle—structures include the ear lobe and cartilage. The external ear also consists of the **external auditory canal**, whose function is to transmit sound waves to the **eardrum** (also called the tympanic membrane). The external auditory canal gathers sound from outside the body and transmits it to the middle ear. This canal accumulates ear wax that typically self-cleans through daily chewing, grinding, and yawning motions (Sevy et al., 2023).

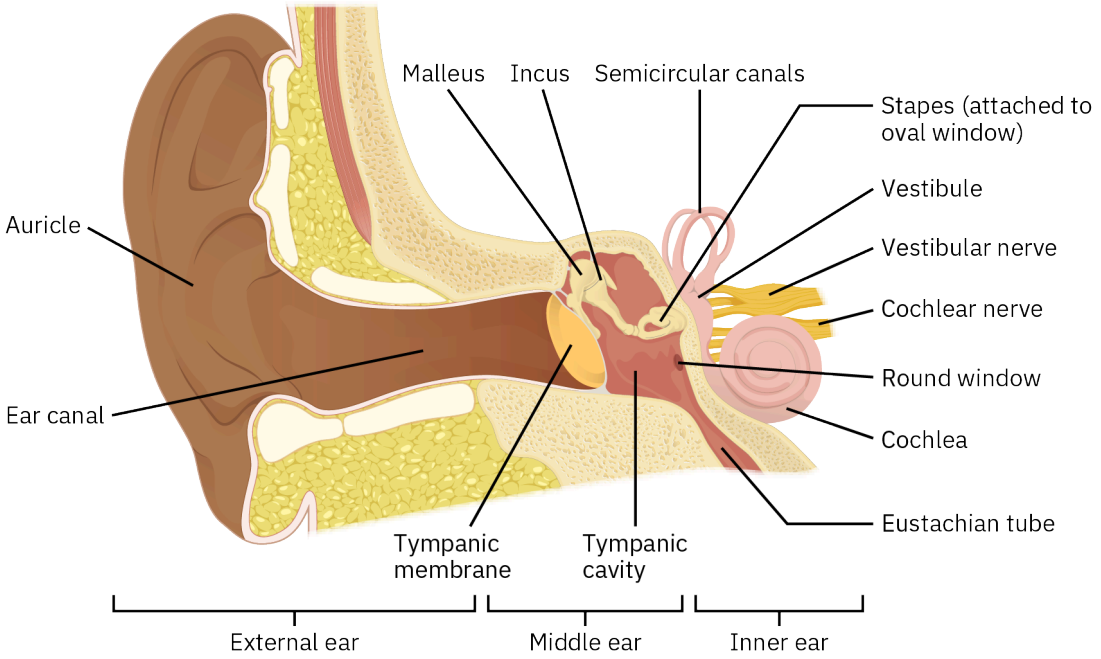


FIGURE 39.2 Structures of the ear include the external ear, middle ear, and inner ear. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

The tympanic membrane is the window from the outer ear into the middle ear. The middle ear consists of the tympanic membrane, **tympanic cavity**, and **ossicles**, which include three small bones: the **malleus**, **incus**, and **stapes**. The purpose of the middle ear is to transmit sound from the tympanic membrane to the inner ear. The tympanic cavity surrounds the three ossicles. The malleus, incus, and stapes transmit oscillatory vibrations from one small bone to another; the delicate stapes sends sound to the inner ear in a highly coordinated relay system. The tympanic membrane can rupture from infection, barotrauma, or the use of cotton swabs.

The **Eustachian tube** connects the middle ear to the back of the nose. It has three major functions:

- To protect the middle ear from infection
- To equalize air pressure on both sides of the eardrum for normal vibration
- To drain secretions from the middle ear

The inner ear is well protected within the temporal bone of the skull. The inner ear consists of the cochlea, the semicircular canals, and the vestibular and cochlear nerves. The cochlea translates sound waves into electrical impulses through mechanical stimulation of tiny hair cells that the brain can then interpret to recognize sounds. The semicircular canals sense head rotations to allow proprioception—the body's ability to sense movement, action, and location—and balance. These canals contain fluid known as lymph and must be clear of debris such as small crystals called **otoliths** (Casale et al., 2023; Wang et al., 2020).

The inner ear is part of the central nervous system (CNS). Therefore, clients' complaints about hearing can also be a sign of a more serious CNS disease process. The nurse should listen carefully to the client's description of hearing issues and communicate concerns with the provider. Muffled hearing can represent a range of concerns from ear wax buildup to multiple sclerosis or neurosyphilis (Ramchandani et al., 2020). The nurse must also be aware of the ears' structure and function, both within the parameters of normal function and when the client sustains a serious head injury or barotrauma.

LINK TO LEARNING

The Ear

Access multimedia content (https://openstax.org/books/pharmacology/pages/39-1-introduction-to-the-ears)
This 4-minute client education video describes the three parts of the ear: the external ear, the middle ear, and the inner ear.

Ear Disorders

This section describes common ear disorders for which pharmacological drops or solutions are prescribed. Selected common ear conditions for which systemic medications are prescribed will be reviewed as well.

Eustachian Tube Dysfunction and Post-Viral Syndrome

Barotrauma can result in a ruptured eardrum due to Eustachian tube dysfunction, which occurs when the air pressure in the middle ear does not equalize with ambient pressure. This can occur with sudden pressure changes, such as when flying or scuba diving. A ruptured eardrum can heal spontaneously or may require surgical intervention (Cleveland Clinic, 2022a). The Eustachian tube can become blocked during and after an upper respiratory infection as well. After an upper respiratory infection, the Eustachian tube may remain swollen, causing pain, muffled sound, or a feeling of fullness in the ear.

Tinnitus

Tinnitus is an ear disorder characterized by ringing or other annoying sounds in the ear. Tinnitus can be age-related, exacerbated by loud noises, or a result of circulation issues. Some medications can cause tinnitus, and hearing may not always fully return after stopping the medication. Medications associated with tinnitus include nonsteroidal anti-inflammatory drugs (NSAIDs), some antibiotics, anticancer medications, and antidepressants (Kim et al., 2021). The mechanism of these intrusive sounds is related to damaged hairs in the cochlea. Although there is no cure for tinnitus, there are treatments—including sound generators and stress management—that can help clients better cope with distracting sounds (Cleveland Clinic, 2022b; National Institute on Deafness and Other Communication Disorders, n.d.).

Ménière's Disease

Ménière's disease occurs when there is excess fluid in the inner ear. The cause is largely unknown. Ménière's disease can have a hereditary component, or it can be triggered by viral or bacterial pathogens. This condition is characterized by hearing loss, vertigo, increased sweating, nausea, and vomiting. The nurse must implement fall precautions when caring for a client with Ménière's disease because vertigo can predispose them to falls, including falls with injuries. There is no cure for Ménière's disease, and though it does not affect life expectancy, it interferes with the client's quality of life. Corticosteroids and antihistamines are offered as potential treatments and have varying effects (Webster et al., 2023).

Otitis Externa

Otitis externa (also known as swimmer's ear) is an inflammation and/or infection of the external ear canal characterized by itchiness, pain, and a red ear canal. Otitis externa occurs in swimmers as well as older adults and those with poorly controlled diabetes. It can be exacerbated by using hearing aids, ear buds, and stethoscopes. The nurse should report client complaints of itchy, painful ear(s) to the provider because an untreated infection can spread to the bones and deep tissues of the ear canal and lead to skull osteomyelitis (Bruschini et al., 2019).

Otitis Media

Otitis media is an inflammation or infection of the middle ear. It typically occurs when the client has a cold, upper respiratory infection, or secondhand smoke exposure. Children are more likely to develop otitis media because of their horizontal Eustachian tube architecture, which increases the likelihood of fluid being trapped, causing an infection. Bottle feeding has been identified as a contributing factor to otitis media. Infants that breastfeed have fewer otitis media infections due to the oligosaccharides that are in breast milk, which function as prebiotics. These substances help infants develop their immune system to fight off infection. In addition, the breastfeeding infant utilizes a sucking motion, resulting in a negative pressure vacuum, thereby reducing pooling of breast milk (Bowatte et al., 2015). Though the incidence of otitis media in adults is less, adults can also develop otitis media. Eustachian

tube edema can narrow the diameter of the tube, allowing fluid to back up to the middle ear.

There are three major types of otitis media: acute otitis media, otitis media with effusion, and chronic otitis media with effusion (Johns Hopkins Medicine, n.d.). Acute otitis media is characterized by ear discomfort, in addition to systemic symptoms including fever and pain. Acute otitis media is frequently treated with systemic antibiotics, otic antibiotics, or a combination of both.

Otitis media with effusion occurs when some fluid remains after an infection has cleared and presents as fullness in the ear. Often decongestants or nasal steroids are prescribed to treat these symptoms. Antibiotics are not appropriate at this stage when no infection persists. The condition may become long-term and return although no infection is present.

Acute otitis media in adults can cause significant complications; therefore, adults are treated with antibiotic therapy (Limb et al., 2023). In general, antibiotic therapy is used more judiciously in children to avoid antibiotic resistance and side effects.

Benign Paroxysmal Positional Vertigo

Benign paroxysmal positional vertigo (BPPV) is a condition of the inner ear where otoliths—crystals of calcium carbonate—migrate into the inner ear fluid and cause a false sense of spinning. Otolith displacement occurs in older adults and those with a history of a blow to the head. BPPV is characterized by dizziness and a spinning sensation and may result in nausea and vomiting. Long after a head trauma, these symptoms can be triggered by a changing head position or keeping the head in one position for an extended period. Episodes can last for a few minutes and are disconcerting to the client, who is at risk of falling.

SPECIAL CONSIDERATIONS

Candida auris

Nurses must be aware of an emerging deadly fungal infection of the ear known as *Candida auris*. This fungal infection was first found in a Japanese person's ear canal in 2009. Since then, there have been more than 3,000 systemic cases in the United States and more than 7,000 cases where the fungus has been found but has not yet caused infection (Centers for Disease Control and Prevention, 2023a, 2023b). *C. auris* must be reported to the Centers for Disease Control and Prevention (CDC) for tracking. Cases in the United States have occurred in health care settings largely among immunocompromised clients. Current treatment includes a drug class, echinocandins, that act on the *Candida* species. Echinocandins include anidulafungin (Eraxis), caspofungin (Cancidas), and micafungin (Mycamine).

(Source: Cândido et al., 2020)

Communicating with a Client with Hearing Impairment

There are different causes of hearing loss—including congenital hearing loss, aging, prolonged exposure to noise, and trauma—that are outside of the scope of this chapter. However, when treating clients with otic medications, the client's hearing may be impaired by these medications or by the underlying ear condition the nurse is treating. The following guidelines can assist the nurse when working with these clients (UCSF Health, n.d.):

- Face the client with the hearing impairment directly when communicating.
- Refrain from talking while in another room or area away from the client.
- Do not shout; rather, speak slowly, clearly, and distinctly.
- Pause between concepts to ensure you are understood before continuing.
- If the hearing-impaired client does not seem to understand a word or phrase, rephrase the message.
- Avoid interrupting the client.
- Provide the client with written information such as a schedule and directions and ask them to repeat the specifics.

39.2 Otic Anti-inflammatories and Anti-infectives

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 39.2.1 Identify the characteristics of anti-inflammatory and anti-infective drugs used to treat ear disorders.
- 39.2.2 Explain the indications, actions, adverse reactions, and interactions of anti-inflammatory and anti-infective drugs used to treat ear disorders.
- 39.2.3 Describe nursing implications of anti-inflammatory and anti-infective drugs used to treat ear disorders.
- 39.2.4 Explain the client education related to anti-inflammatory and anti-infective drugs used to treat ear disorders.

Otic Anti-inflammatories

Anti-inflammatory drugs block substances in the body that cause inflammation. Otic anti-inflammatories are used for the treatment of superficial bacterial infections of the external auditory canal (i.e., otitis externa) caused by susceptible organisms. Anti-inflammatory medications frequently are administered in combination with antibiotics. A treatment response should occur within 48–72 hours, otherwise the provider should reassess (Medina-Blasini & Sharman, 2023).

Adverse Effects and Contraindications

Adverse effects are rare; however, clients can experience allergic reactions characterized by rash, itching, and redness. Dizziness may occur. Prolonged usage can result in a superinfection that requires additional medications to resolve.

Table 39.1 is a drug prototype table for otic anti-inflammatories featuring neomycin and polymyxin B sulfates, and hydrocortisone otic solution (Cortisporin). It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antibacterial and anti-inflammatory **Mechanism of Action** Suppresses the inflammatory response (hydrocortisone) Works against susceptible organisms (anti-infectives)	**Drug Dosage** *Adults:* 4 drops of medication instilled in the ear 3–4 times daily, not to exceed 10 days. *Children:* 3 drops of medication instilled in the ear 3–4 times daily, not to exceed 10 days. Each mL contains: neomycin sulfate 3.5 mg, polymyxin B 10,000 units, and hydrocortisone 10 mg (1%).
Indications For the treatment of superficial bacterial infections of the external auditory canal (i.e., otitis externa) caused by susceptible organisms For the treatment of infections of mastoidectomy **Therapeutic Effects** Reduces ear pain Reduces bacterial infection Decreases inflammation	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Local, adverse reactions (most common are burning, itching, irritation, and dryness) Stinging and burning (if medication reaches the middle ear) Hearing loss (with prolonged use—treatment should be limited to 10 days)	**Contraindications** Perforated eardrum Fungal or viral lesions Hypersensitivity to any medication components

TABLE 39.1 **Drug Prototype Table: Neomycin and Polymyxin B Sulfates, and Hydrocortisone Otic Solution** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking otic anti-inflammatories:

- Recognize and monitor for serious and other potential side effects. Rarely, anaphylaxis can occur with the first dose.
  - Clients with latex allergies may need to use an alternative (latex-free) dropper for administration.
- Perform hand hygiene before administering otic anti-inflammatory medication.
- Educate the client on ear position and time to remain in a lying position after instillation.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an otic anti-inflammatory should:

- If this is the first time using these drugs, administer with another person present for assistance in case a serious allergic reaction occurs.
- Always wash their hands before handling a bottle of otic drops and be mindful of the bottle cap to ensure that it remains as germ-free as possible.
- Roll the bottle of otic drops between their hands for a few moments to warm the drops. Instillation of cold drops can cause dizziness.
- Administer the drops with the pinna in an upward position; it should remain up during otic drop instillation.
- Keep the ear facing up for about 5 minutes for the drop(s) to bathe the ear canal and minimize the amount of medication leakage (Mayo Clinic, 2023).
- Use a latex-free dropper if they have a latex allergy.

The client taking an otic anti-inflammatory *should not:*

- Heat the drops above body temperature because administering drops that are too warm can damage the ear canal.
- Drive or operate machinery until any occurrences of dizziness and vertigo have subsided.
- Use cotton swabs in their ears due to the risk of perforation and further irritation and injury (Cleveland Clinic, 2022a).
- Use the medication for longer than the prescribed duration.

Otic Topical Anti-infectives

Otic anti-infectives are indicated for clients who have otitis externa. Topical anti-infectives are prescribed to treat bacterial infections but are ineffective for viral infections. If the infection does not improve after 1 week of treatment, cultures and susceptibility tests should be repeated to verify the identity of the organism and to determine whether the therapy should be changed.

Table 39.2 lists common otic topical anti-infectives and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Ciprofloxacin 0.3% and dexamethasone 0.1% (Ciprodex)	*For the treatment of acute otitis media in adults and acute otitis media in children with tympanostomy tubes:* 4 drops instilled into the affected ear twice daily for 7 days.
Ciprofloxacin 0.2% and hydrocortisone 1% (Cipro HC)	*For the treatment of acute otitis externa due to susceptible organisms:* *For clients ≥1 year:* 3 drops instilled into the affected ear(s) twice daily for 7 days. Maximum dose: 6 drops daily to affected ear(s).
Ofloxacin (Floxin)	*For the treatment of otitis media and acute otitis media in children with tympanostomy tubes:* *For clients 1–12 years:* 5 drops (0.75 mg) in the affected ear(s) twice daily for 10 days. *For the treatment of long-term suppurative otitis media with perforated tympanic membranes:* *For clients 12 and older:* 10 drops (1.5 mg) in the affected ear(s) twice daily for 14 days. *For the treatment of otitis externa due to Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus:* *For clients 6 months to 12 years:* 5 drops (0.25 mL, 0.75 mg ofloxacin) in the affected ear(s) once daily for 7 days. *For clients 13 years and older:* 10 drops (0.5 mL, 1.5 mg ofloxacin) in the affected ear(s) once daily for 7 days.

TABLE 39.2 **Drug Emphasis Table: Otic Topical Anti-infectives** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects of otic anti-infectives may include ear itching, fungal ear superinfection, earache, tinnitus, and transient hearing loss. Contraindications to taking otic anti-infectives include a history of hypersensitivity to any ingredient in the medication.

Table 39.3 is a drug prototype table for otic topical anti-infectives featuring ciprofloxacin 0.2%/hydrocortisone 1%. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Otic topical anti-infective **Mechanism of Action** Kills bacteria Reduces inflammatory response that accompanies infection	**Drug Dosage** *For clients ≥1 year:* 3 drops instilled into the affected ear(s) twice daily for 7 days. Maximum dose: 6 drops daily to affected ear(s).
Indications For the treatment of superficial bacterial infections of the external auditory canal (i.e., otitis externa) caused by susceptible organisms, including pseudomonas and staphylococcus For the treatment of infections of mastoidectomy **Therapeutic Effects** Eases discomfort Reduces inflammation Treats infection	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Ear itching Fungal ear superinfection Earache Tinnitus Transient hearing loss Dizziness	**Contraindications** A history of hypersensitivity to ciprofloxacin

TABLE 39.3 **Drug Prototype Table: Ciprofloxacin 0.2% and Hydrocortisone 1%** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking otic anti-infectives:

- Recognize and monitor for serious and potential side effects, primarily a rash or any evidence of hypersensitivity to quinolones. Anaphylaxis can occur. Clients with latex allergies need to use a latex-free dropper to administer.
- Perform hand hygiene before administering.
- Educate the client on ear position and time to remain in a lying position after instillation.
- Monitor complete blood count, if ordered, for decreased eosinophils.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an otic topical anti-infective should:

- Report ear pain or worsening of itching to the health care provider; they may need an ear swab to test for superinfection if used for an extended period.
- Always wash their hands before handling a bottle of otic drops and be mindful of the bottle cap to ensure that it remains as germ-free as possible.
- Roll the bottle of otic drops between hands for a few moments to warm the drops. Instillation of cold drops can cause dizziness.
- Administer the drops with the pinna in an upward position; it should remain up during otic drop instillation.
- Keep the ear facing up for about 5 minutes for the drop(s) to bathe the ear canal and minimize the amount of medication leakage (Mayo Clinic, 2023).

The client taking an otic topical anti-infective *should not:*

- Warm the drops to greater than their body temperature because this can damage the ear.
- Drive or operate machinery until any occurrences of dizziness have subsided.
- Use cotton swabs in their ears due to the risk of perforation and further irritation and injury (Cleveland Clinic, 2022a).

CLINICAL TIP

Topical Otic Medication Administration

Access multimedia content (https://openstax.org/books/pharmacology/pages/39-2-otic-anti-inflammatories-and-anti-infectives)
This video from Tacoma Community College demonstrates the proper procedure for administering otic medication to an adult client.

For pediatric clients, review these instructions from the American Academy of Pediatrics (https://openstax.org/r/healthychildren).

Systemic Anti-infectives for Infections of the Ear

Systemic otic anti-infectives are indicated for clients who have otitis media. Acute otitis media in adults can cause significant complications; therefore, most adults are treated with antibiotic therapy (Limb et al., 2023). Antibiotic therapy is used more judiciously in children to avoid antibiotic resistance and side effects. High-dose amoxicillin is the first-line choice for both children and adults (Danishyar & Ashurst, 2023). If high-dose amoxicillin is not effective, high-dose amoxicillin-clavulanate is the second-line treatment. For clients with penicillin allergies or non-responders, azithromycin or cefdinir are two alternatives that can be considered.

Table 39.4 lists common otic systemic anti-infectives and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Amoxicillin (Amoxil, Trimox)	*Severe infections:* *Adults:* 875 mg orally every 12 hours or 500 mg orally every 8 hours. *Children <3 months:* Amoxicillin 30 mg/kg daily for a 10-day course, given in 2 divided doses. *Children ≥3 months:* Amoxicillin 45 mg/kg daily for a 7-day course, given in 2 divided doses.
Amoxicillin-clavulanate (Augmentin)	*Severe infections:* *Adults:* One 875 mg amoxicillin/125 mg potassium clavulanate tablet orally every 12 hours or one 500 mg amoxicillin/125 mg potassium clavulanate tablet orally every 8 hours. *Children >40 kg:* Use adult dosing. *Children ≥3 months and weighing <40 kg:* 45 mg/kg daily orally every 12 hours or 40 mg/kg daily every 8 hours (using 200 mg amoxicillin/28.5 mg potassium clavulanate mg per 5 mL or 400 mg amoxicillin/57 mg potassium clavulanate per 5 mL oral suspension). *Children <3 months:* 30 mg/kg daily orally every 12 hours (using 125 mg amoxicillin/31.25 mg potassium clavulanate mg per 5 mL oral suspension).
Azithromycin (Zithromax)	*For children with acute otitis media (using oral suspension 500 mg in 5 mL):* *Children ≥6 months:* 30 mg/kg orally as a single dose, or 10 mg/kg once daily for 3 days, or 10 mg/kg as a single dose on day 1 followed by 5 mg/kg daily on days 2 through 5.
Cefdinir (Omnicef)	*For children with acute otitis media (using either 125 mg per 5 mL or 250 mg per 5 mL oral suspension):* *Children 6 months through 12 years:* 7 mg/kg orally every 12 hours for 5–10 days or 14 mg/kg orally every 24 hours for 10 days.

TABLE 39.4 Drug Emphasis Table: Otic Systemic Anti-infectives (sources: https://dailymed.nlm.nih.gov/dailymed/; Bode, 2020)

Adverse Effects and Contraindications

Systemic antibiotics can lead to diarrhea and possibly pseudomembranous colitis and *Clostridium difficile* infection. Symptoms of *C. difficile* can range from mild to life-threatening and may require hospitalization and extended

therapy. Antibiotic-related diarrhea can occur up to 2 months after ceasing antibiotic therapy. Antibiotics can cause allergic reactions, especially in clients with other sensitivities.

Table 39.5 is a drug prototype table for otic systemic anti-infectives featuring amoxicillin. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Systemic anti-infective; analog of ampicillin **Mechanism of Action** Bactericidal antibiotic effective for many gram-positive and gram-negative bacteria	**Drug Dosage** *Severe infections:* *Adults:* 875 mg orally every 12 hours or 500 mg orally every 8 hours. *Children <3 months:* Amoxicillin 30 mg/kg/day for a 10-day course, given in 2 divided doses. *Children ≥3 months:* Amoxicillin 45 mg/kg/day for a 7-day course, given in 2 divided doses.
Indications For the treatment of acute otitis media and sinusitis **Therapeutic Effects** Treats infection	**Drug Interactions** Probenecid Oral estrogen/progesterone contraceptives **Food Interactions** No significant interactions
Adverse Effects Sensitivity reactions, particularly in clients allergic to penicillin Diarrhea including from *Clostridium difficile* Abnormal liver function tests	**Contraindications** Known hypersensitivity to penicillin

TABLE 39.5 **Drug Prototype Table: Amoxicillin** (sources: https://dailymed.nlm.nih.gov/dailymed/; Bode, 2020)

Nursing Implications

The nurse should do the following for clients who are taking systemic anti-infectives for otic conditions:

- Recognize and monitor for serious and potential side effects including signs of allergic reactions and new onset of diarrhea.
- Follow dosing instructions carefully, particularly with amoxicillin-clavulanate (Augmentin). Different forms of Augmentin contain different amounts of amoxicillin but the same amounts of clavulanic acid, so the strengths are not interchangeable. For example, two 250 mg Augmentin tablets are not the equivalent of a 500 mg tablet. If a client is prescribed 500 mg, the client must take the 500 mg tablet, not two 250 mg tablets.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an otic systemic anti-infective should:

- Report episodes of diarrhea to their health care provider.
- Take all their antibiotic(s) as prescribed.
- Keep follow-up appointments.

The client an otic systemic anti-infective *should not:*

- Share antibiotics with others.

39.3 Otic Antihistamines, Decongestants, and Cerumenolytics

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 39.3.1 Identify the characteristics of antihistamines, decongestants, and cerumenolytic drugs used to treat ear disorders.
- 39.3.2 Explain the indications, actions, adverse reactions, and interactions of antihistamines, decongestants, and cerumenolytic drugs used to treat ear disorders.
- 39.3.3 Describe nursing implications of antihistamines, decongestants, and cerumenolytic drugs used to treat ear disorders.
- 39.3.4 Explain the client education related to antihistamines, decongestants, and cerumenolytic drugs used to treat ear disorders.

Antihistamines

Antihistamines decrease congestion of mucous membranes, which might decrease corresponding obstruction of tubes within the ear. Antihistamines are used primarily to treat allergies and manage symptoms related to upper respiratory infections. Selected first-generation antihistamines are included here. Please refer to Upper Respiratory Disorder Drugs for a more detailed review of antihistamine medications.

Table 39.6 lists common antihistamines for ear disorders and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Chlorpheniramine maleate (Chlor-Trimeton)	*Adults and children ≥12 years:* 4 mg tablet orally every 4–6 hours as needed. Maximum dose: 6 tablets/day. *Children 6–12 years:* ½ of a 4 mg tablet every 4–6 hours. Maximum dose: 3 tablets/day. *Children <6 years:* Do not use.
Cetirizine hydrochloride (Zyrtec)	*Adults and children >6 years:* 10 mg once daily; do not take more than 10 mg in 24 hours. A 5 mg product may be appropriate for less severe symptoms.
Diphenhydramine (Benadryl)	*Adults and children >12 years:* 25–50 mg orally every 4–6 hours as needed. Maximum of 6 doses in 24 hours. *Children 6–12 years:* 25 mg orally every 6 hours as needed not to exceed 4 doses in 24 hours. *Children <6 years:* Do not use.
Loratadine (Claritin)	*Adults and children >6 years:* 10 mg once daily; do not take more than 10 mg in 24 hours.

TABLE 39.6 **Drug Emphasis Table: Antihistamines** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

The use of antihistamines in clients with hypertension can further increase blood pressure. Clients at risk for cardiac dysrhythmia, such as a prolonged QT interval on an electrocardiogram, should communicate with their provider before taking a first-generation antihistamine like diphenhydramine due to potential proarrhythmic effects (Williamson, 2022). Since antihistamines have a drying effect, clients with glaucoma and urinary retention should avoid taking an antihistamine. Antihistamines exacerbate the sedating effects of tranquilizers and alcohol, which can lead to respiratory depression and injuries from falls. Due to antihistamines' blocking effects on acetylcholine, they can also cause constipation.

Table 39.7 is a drug prototype table for first-generation antihistamines featuring diphenhydramine. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antihistamine **Mechanism of Action** Stops chemicals in the immune system that trigger allergy-related symptoms	**Drug Dosage** *Adults and children >12 years:* 25–50 mg orally every 4–6 hours as needed. Maximum of 6 doses in 24 hours. *Children 6–12 years:* 25 mg orally every 6 hours as needed not to exceed 4 doses in 24 hours. *Children <6 years:* Do not use.
Indications For the treatment of symptoms associated with the common cold or allergic rhinitis including sneezing, rhinorrhea, itching of the nose or throat, and itchy, watery eyes **Therapeutic Effects** Temporary relief of rhinitis, sneezing, itchy eyes, nose, or throat due to upper respiratory inflammation	**Drug Interactions** Sedatives and tranquilizers with sedative effects Alcohol **Food Interactions** No significant interactions
Adverse Effects Drowsiness Dry mouth Dizziness Headache Constipation	**Contraindications** Hypertension Cardiovascular arrhythmia History of glaucoma Urinary retention Caution: Operating a motor vehicle or machinery

TABLE 39.7 **Drug Prototype Table: Diphenhydramine** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking antihistamines:

- Monitor the client for potential side effects including drowsiness or oversedation.
- Educate the client to refrain from driving or operating machinery while taking these medications because they can cause drowsiness and impair cognitive function.
- Educate the client to guard against potential constipation by increasing fiber and fluid intake.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an antihistamine should:

- Be aware that antihistamines can cause drowsiness.
- Keep fluids or hard candy on hand to manage symptoms of dry mouth.
- Maintain adequate fiber and fluid intake to reduce likelihood of experiencing constipation.

The client taking an antihistamine *should not:*

- Drive or operate machinery when feeling drowsy.

Decongestants

Decongestants are medications that shrink swollen blood vessels and tissues in the nose to reduce nasal congestion, which can facilitate drainage to relieve ear congestion. They can be used to manage symptoms of an upper respiratory illness or prophylactically when flying to decrease discomfort associated with changes in air pressure. These medications should be used with caution in clients with a history of heart disease, thyroid disorder, diabetes, or hypertension. Alternatives include using saline nasal spray, room humidification, or being in a room with

a hot shower running that creates a steamy environment. (For more detailed information on decongestants, please see Upper Respiratory Disorder Drugs.)

Adverse Effects and Contraindications

Decongestants should be avoided in clients who have a history of hypertension or heart disease because these medications can raise blood pressure and stimulate the heart. They can increase intraocular pressure in clients who have glaucoma; particularly among clients with benign prostatic hypertrophy, decongestants can inhibit the ability to void.

Table 39.8 is a drug prototype table for decongestants featuring pseudoephedrine (Sudafed). It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Nasal decongestant **Mechanism of Action** Indirectly stimulates alpha-adrenergic receptors, causing vasoconstriction	**Drug Dosage** *Regular-release tablets or liquid-filled capsules:* *Adults and children ≥12 years:* 60 mg orally every 4–6 hours; maximum dose: 240 mg daily. *Children 6–11 years:* 30 mg orally every 4–6 hours; maximum dose: 120 mg daily. *12-hour extended-release tablets:* *Adults:* 120 mg orally (1 tablet) every 12 hours; maximum dose: 240 mg daily. *24-hour extended-release tablets:* *Adults:* 240 mg orally every 24 hours; maximum dose: 240 mg daily. *Oral solution containing 15 mg or 30 mg pseudoephedrine per 5 mL:* *Adults:* 60 mg orally every 4–6 hours; maximum dose: 240 mg daily.
Indications For temporary relief of sinus congestion and pressure For temporary relief of nasal congestion due to a cold or other upper respiratory allergies **Therapeutic Effects** Eases discomfort and allergy symptoms	**Drug Interactions** Monoamine oxidase inhibitors (MAOIs) **Food Interactions** No significant interactions
Adverse Effects Insomnia Anxiety Elevated blood pressure Elevated glucose Increased intraocular pressure Worsening glaucoma	**Contraindications** Heart disease Hypertension Thyroid disease Diabetes Urinary retention due to enlarged prostate gland

TABLE 39.8 **Drug Prototype Table: Pseudoephedrine** (sources: https://dailymed.nlm.nih.gov/dailymed/; Glowacka & Wiela-Hojenska, 2021)

Nursing Implications

The nurse should do the following for clients who are taking decongestants:

- Monitor the client's blood pressure, especially if they have a history of hypertension, and report elevated readings to the provider.
- Monitor the client's blood glucose levels if the client has diabetes and report elevated readings to the provider.
- Be aware that decongestants can raise intraocular pressure. This can be especially concerning for clients with glaucoma. Assess the client for any visual changes, eye pain or irritation, or headache. Report any findings to the provider.

- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a decongestant should:

- Talk to their health care provider before starting a decongestant, especially if underlying health conditions exist.
- Check their blood pressure while taking decongestants if they have prehypertension/hypertension.
- Monitor their blood glucose levels while taking decongestants if they have prediabetes/diabetes.
- If they have glaucoma, check with their ophthalmologist about decongestant use and report any visual changes, eye pain, or headache.
- Take decongestants for the shortest amount of time possible and do not take multiple decongestants from different decongestant classes.
- Clients taking monoamine oxidase inhibitors (MAOI) and decongestants can experience hypertensive crisis (Edinoff et al., 2022).

Otic Cerumenolytics

Typically, the body naturally expels earwax; however, sometimes a buildup occurs requiring the administration of medication to facilitate its removal. A commonly prescribed **cerumenolytic** is carbamide peroxide (Debrox). The drops work by releasing oxygen to soften and encourage spontaneous extrusion of cerumen. They also have a weak antibacterial effect.

Table 39.9 is a drug prototype table for otic cerumenolytics featuring carbamide peroxide. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Otic cerumenolytic **Mechanism of Action** Contains peroxide, which creates foaming that softens and breaks apart the wax	**Drug Dosage** *Adults and children ≥12 years:* 5–10 drops of the 6.5% solution in ear twice daily for up to 4 days.
Indications To soften and encourage spontaneous extrusion of cerumen **Therapeutic Effects** Facilitates ear wax removal	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Effects Ear discomfort Transient loss of hearing Dizziness Local irritation	**Contraindications** Ear infection Ear pain Ear rash Recent ear surgery Eardrum dysfunction

TABLE 39.9 **Drug Prototype Table: Carbamide Peroxide** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking an otic cerumenolytic:

- Educate clients about the benefits of ear wax and how the ear is a self-cleaning organ.
- Examine the client's ears before treatment for any evidence of drainage or other symptoms that would prevent safe administration. Consult with the provider if concerning finding are present.

- Examine the client's ears after treatment using an otoscope to determine effectiveness of treatment. If no results are obtained, notify the provider for further evaluation.
- After administering the medication, any remaining wax can be removed by gentle irrigation with warm water.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking an otic cerumenolytic should:

- Use in consultation with their provider.
- Pull the pinna in an upward fashion to instill drops.
- Remain in a lying position for 5 minutes after instillation.
- Report ear discomfort, dizziness, or local discomfort.

The client taking an otic cerumenolytic *should not:*

- Instill cerumenolytic drops after recent ear surgery or if there is eardrum dysfunction.

Chapter Summary

This chapter provided an overview of the structure and functions of the ear, along with an exploration of various medications used to treat ear-related issues. The ear is a complex organ divided into three main parts: the outer ear, middle ear, and inner ear. The outer ear includes the pinna and ear canal, responsible for collecting and transmitting sound waves. The middle ear contains the ossicles (small bones), which amplify sound, and the inner ear houses the cochlea, responsible for converting sound into electrical signals sent to the brain.

Several types of medications related to ear ailments were discussed. Otic anti-inflammatories are used to reduce inflammation and relieve pain in the ear, particularly for conditions like otitis externa. Anti-infectives are essential in treating ear infections by targeting bacteria or fungi causing the issue. Oral antihistamines help alleviate allergy-related ear symptoms, such as itching and congestion. Decongestants are used to reduce swelling and congestion in the Eustachian tube, aiding in the treatment of middle ear problems. Lastly, cerumenolytics are agents designed to soften and loosen earwax (cerumen) buildup, facilitating its safe removal from the ear canal.

Key Terms

antihistamine medication that relieves allergy symptoms, including stuffy nose and watery eyes

barotrauma trauma that occurs when the air pressure in the middle ear does not equalize with ambient pressure

benign paroxysmal positional vertigo (BPPV) a condition of the inner ear where otoliths migrate into the inner ear fluid, causing a false sense of spinning

cerumenolytic a medication that softens and loosens ear wax to ease removal

cochlear nerve one of two bifurcated nerves branching from the vestibulocochlear nerve; it transmits signals from the cochlea to the temporal lobe in the brain so sound can be heard

decongestant a medication that shrinks swollen blood vessels and tissues in the nose to reduce nasal congestion and aid in relieving ear congestion

eardrum a thin flap that separates the external or outer ear and middle ear; it vibrates to sound, which initiates an intricate relay throughout the ear structures traversing from the bones of the middle ear to the inner ear's cochlea where hearing occurs; also known as the tympanic membrane

Eustachian tube connects the middle ear to the nasal-sinus cavity

external auditory canal path from the external ear to the middle ear

incus one of three small bones in the middle ear; it transmits vibrations from the malleus to the stapes

malleus one of three small bones in the middle ear; it is located closest to the tympanic membrane and transmits auditory oscillations to the incus

Ménière's disease occurs when fluid accumulates in the inner ear, which can be triggered by allergies, head injury, migraine headache; or viral infection; characterized by vertigo and hearing loss

ossicles three small bones in the middle ear, consisting of the malleus, incus, and stapes, that transmit oscillatory vibrations from one small bone to another; the stapes sends sound to the inner ear in a highly coordinated relay system

otitis externa inflammation and/or infection of the external ear canal characterized by itchiness, pain, and a red ear canal

otitis media an inflammation or infection of the middle ear; also known as swimmer's ear

otolith a calcium carbonate crystal that normally resides in the base of the semicircular canal that can dislodge into the semicircular canal fluid and lead to bouts of vertigo

stapes one of three small bones in the middle ear; it moves fluid into the cochlea in the inner ear

tinnitus an ear disorder characterized by ringing or other annoying sounds in the ear

tympanic cavity an air-filled compartment separated from the external ear by the tympanic membrane; it communicates with the pharynx via the Eustachian tube

vestibular nerve one of two bifurcated nerves branching from the vestibulocochlear nerve; it controls motion and position

vestibulocochlear nerve the eighth cranial nerve, which transmits sound from the inner ear to the auditory cortex in the temporal lobe of the brain.

Review Questions

1. The nurse teaches parents of school-age children that which structure protects the middle ear from infection?

a. External auditory canal
b. Eustachian tube
c. Tympanic membrane
d. Ossicles

2. The nurse is caring for a client who has an upper respiratory illness but is getting ready to travel by plane. Which medication should the nurse anticipate being prescribed to minimize ear-related problems during the flight?
a. Diphenhydramine
b. Amoxicillin
c. Pseudoephedrine
d. Carbamide peroxide

3. Which instruction should the nurse give to a client to reduce tinnitus?
a. Take a nonsteroidal anti-inflammatory drug.
b. Reduce background sound.
c. Increase caffeine intake.
d. Decrease sodium intake.

4. Which communication technique is most effective for the nurse to use when communicating with a client with hearing impairment?
a. Look directly at the client and use a loud voice.
b. Move on to the next topic if the client does not understand you.
c. Instruct the client to read your lips.
d. Avoid interrupting the client with a hearing impairment.

5. Which of the following is a proper technique regarding otic antibiotics?
a. Warm the drops to above body temperature.
b. Instill the ear drops while seated comfortably.
c. Avoid touching the tip of the dropper to any surface.
d. Store ear drops in the refrigerator.

6. Which assessment finding indicates to the nurse that a client receiving an otic antibiotic may have a resistant infection, also known as a superinfection?
a. Low blood pressure and elevated heart rate
b. Tearing eyes on the affected side
c. Pain and ear itching
d. Headache and nausea

7. Which adverse effect should the nurse caution the client taking amoxicillin-clavulanate to expect?
a. The client could experience ototoxic side effects.
b. The client should be careful when driving at night.
c. The client could experience diarrhea.
d. The client could develop hearing loss.

8. Which instruction should the nurse give to a client with diabetes who is taking a decongestant for relief from sinus and ear congestion caused by an upper respiratory infection?
a. Increase daily insulin while taking the decongestant.
b. Decrease daily insulin while taking the decongestant.
c. Regularly check serum glucose while taking the decongestant.
d. Taper the decongestant before stopping the medication.

9. Which action should the nurse take to evaluate the effectiveness of carbamide peroxide administered to a

client's ear?

a. Take the client's temperature.
b. Examine the ear canal.
c. Check the client's hearing.
d. Ask the client to rate their pain.

10. Which diagnosis does the nurse anticipate in the client who reports hearing loss, vertigo, nausea, and vomiting?

a. Ménière's disease
b. Tinnitus
c. Otitis externa
d. Otitis media

CHAPTER 40
Dermatologic Disorder Drugs

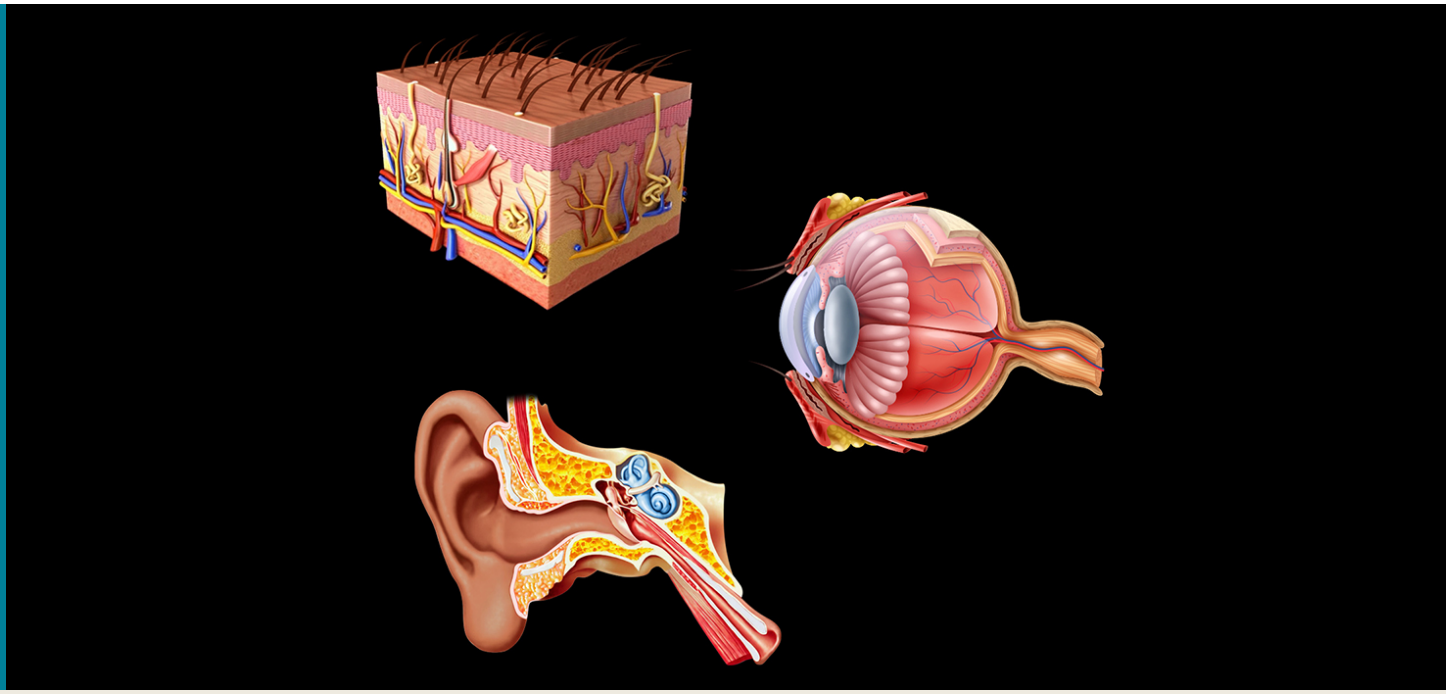


FIGURE 40.1 Maintaining clients' health can include understanding pharmacological options that enhance vision, auditory health, and skin wellness. (attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

CHAPTER OUTLINE

INTRODUCTION The skin, in addition to being the largest organ of the body, is a very complex organ that serves as the body's primary defense system. Maintaining healthy skin prevents organisms from entering a host's body to cause infections. Any disruption in the skin's integrity creates an open portal for transmission of disease. In addition to protection, the skin aids in thermoregulation, reception of sensory stimuli, and excretion of wastes. This chapter will explore common disruptions of the skin and their associated treatments that promote healthy skin.

40.1 Introduction to the Skin and Its Function

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 40.1.1 Discuss the skin and its two major layers.
- 40.1.2 Identify the five layers of the epidermis and their purposes.
- 40.1.3 Describe the two layers of the dermis and their purposes.
- 40.1.4 Explain the role of the hypodermis as it relates to the skin and dermatologic disorders.

The **epidermis**, the **dermis**, and the **hypodermis** are the layers that comprise the skin. The foundation of the skin is known as the hypodermis (also subcutaneous tissue or **superficial fascia**). The hypodermis is composed of fatty tissues and membranes that hold the dermis to the underlying muscle (see Figure 40.2).

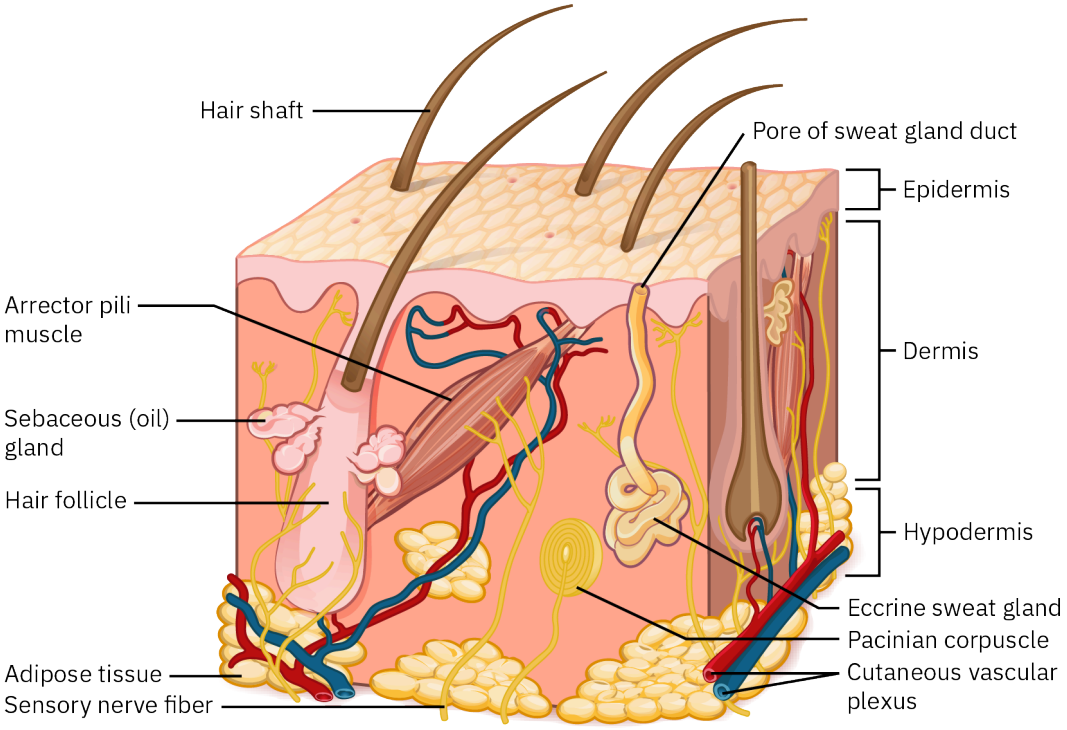


FIGURE 40.2 The three basic skin layers are the epidermis, dermis, and hypodermis. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Above the hypodermis lies the dermis. The dermis is rich in vascularity, nerves, and sensory receptors embedded in a more elastic, collagenous system of fibers. The bottom dermal sublayer—the reticular layer—is much thicker and more vascular than the other skin layers and contains more nerve and sensory functions. The uppermost sublayer—the papillary layer—contains **papillae**, which extend upward into the epidermis to hold the dermis and epidermis together. The papillary layer also contains phagocytes, which act to destroy bacteria that may penetrate the epidermis. New dermal growth pushes skin cells through the dermis and upward into the epidermis.

The epidermis is the outermost layer of skin comprising the external skin surface of humans. Unlike the dermis, the epidermis does not contain blood vessels and nerves, but is composed mainly of cellular sublayers that protect the dermis. The basal layer (stratum basale) is the foundation of the epidermis in areas where the stratum lucidum is not present. (The stratum lucidum is an additional layer that provides a thicker layer of epidermis in areas that need more protection, such as the palms of the hands and soles of the feet.) The basal layer is the only epidermal sublayer that is not made from keratin cells. This layer bonds to the dermis to connect it to epidermal tissues. The remaining sublayers of the epidermis are composed of keratinocytes, cells that are protein based, giving rise to hair, nail, and skin cells that are strong and water-resistant. Just above the basal layer is the spinous layer (stratum spinosum), which is composed of a depth of 8–10 cells that have spiny processes that help to hold the cell layers together. Encompassed in this layer are **Langerhans cells**, which eliminate foreign bacteria and wastes that enter the spinous layer, providing protection from invading organisms.

Human skin has a high mitotic rate and has more rapid cell development and cell death than many other body tissues. In addition to rapid growth, skin cells travel from the dermis through the epidermis until they die and are shed from the outermost skin surface. The third sublayer of the epidermis is the granular layer (stratum granulosum), which is composed of a depth of 3–5 keratinous cells that are flatter and more protein based than the other sublayers. These cells essentially die, leaving behind a fibrous protein layer that gives rise to the fourth layer, the cornified layer (stratum corneum). The cornified layer is the outermost layer that forms the visible, external skin and is 20–30 cells thick (Yousef et al., 2022).

When conditions threaten skin integrity, prompt diagnosis and treatment enable the primary defense of the body systems to remain strong. As skin integrity becomes compromised, bacteria, other organisms, and contaminating substances may enter the body through breaks in the skin. Dermatologic medications assist in healing breaks in the skin, preventing infection, and maintaining healthy skin.

TRENDING TODAY

Dermatologic Diagnosis and Treatment Disparities in People of Color

One issue that has been identified as a barrier to treatment of skin conditions it the correct diagnosis and treatment for people of color. Skin conditions in darker-skinned individuals often present differently than in lighter-skinned individuals. This article from *American Family Physician* (https://openstax.org/r/aafporg) discusses the need for better educating dermatologists in the proper recognition and treatment of skin issues in clients with darker skin (Frazier et al., 2023).

40.2 Acne Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 40.2.1 Identify the characteristics of drugs used to treat acne.
- 40.2.2 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat acne.
- 40.2.3 Describe nursing implications of drugs used to treat acne.
- 40.2.4 Explain the client education related to drugs used to treat acne.

Acne vulgaris (acne) is a skin condition in which **sebum**—dead skin cells—and bacteria accumulate in a skin pore. The pore becomes clogged and allows bacterial growth, which causes the surrounding skin to erupt in skin lesions or vesicles. Although acne is typically considered a condition of adolescents and young adults, occasionally it may continue into adulthood, especially in female clients. Oily skin, hormonal changes, family history, and some medications may cause or exacerbate acne. Acne presents as multiple pustules, papules, or nodules on the skin, particularly on the face but also on the back, upper arms, and trunk (Sutaria et al., 2023). Figure 40.3 shows the development of acne within a pore.

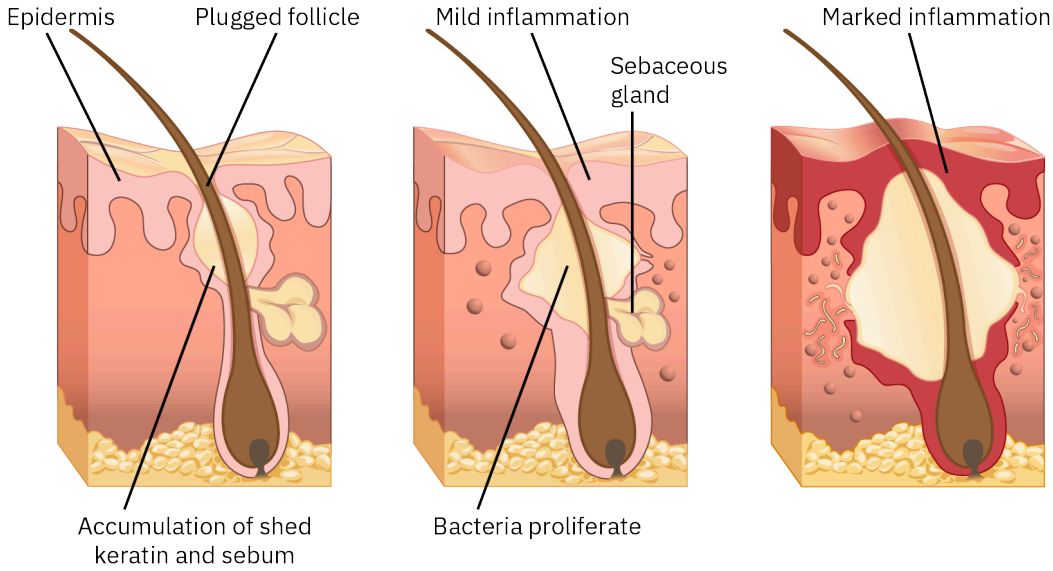


FIGURE 40.3 Acne is a result of overproductive sebaceous glands, which leads to the formation of pustules and inflammation of the skin. (credit: modification of work from *Anatomy and Physiology 2e*. attribution: Copyright Rice University, OpenStax, under CC BY 4.0 license)

Effective treatment of acne begins with proper skin hygiene. In addition to cleansing and exfoliating the skin, treatment also focuses on reducing inflammation and decreasing bacteria on the skin. Both systemic and topical medications are used to manage acne to achieve these goals.

Systemic Acne Drugs

Systemic medications for the treatment of acne consist mainly of oral anti-infectives used to reduce bacterial colonization in skin pores. This reduces inflammation and infection, allowing pustules and lesions to heal while also preventing further development of acne. These anti-infectives include tetracyclines such as tetracycline hydrochloride, minocycline hydrochloride, and doxycycline. Clindamycin, a lincosamide antibiotic, may also be used.

Drugs such as these specifically treat organisms affecting the skin, including streptococcal and staphylococcal bacteria.

Table 40.1 lists common systemic acne drugs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Tetracycline hydrochloride (Sumycin, Panmycin, Acnecycline)	*Oral* *Adults:* 1000 mg/day in divided doses for acute acne; maintenance for acne prevention: 125–500 mg daily. *Children ≥8 years*: 25–50 mg/kg daily, divided into 4 equal doses. *Children <8 years:* Do not administer. *Topical* *3% ointment:* Apply twice daily in a thin layer over the entire affected area.
Minocycline hydrochloride (Minocin, Ximino, Zilxi)	*Oral* *Adults:* Initial dose: 200 mg orally, then 100 mg orally twice daily. *Children ≥8 years:* Initial dose: 4 mg/kg orally, then 2 mg/kg orally every 12 hours. *Children <8 years:* Do not administer. *Topical* *4% foam:* Apply small (cherry-sized) amount to affected areas. Repeat as needed until symptoms resolve. Apply at the same time each day at least 1 hour before bedtime or before bathing, showering, or swimming.
Clindamycin (Cleocin)	*Oral* *Adults:* 150–450 mg orally every 6 hours. *Children:* 8–20 mg/kg daily orally, divided into 3–4 doses. *Topical* *1% topical solution:* Apply thin film to affected areas twice daily.
Doxycycline hyclate (Vibramycin, Doxycin)	*Adults and children ≥45 kg:* Initial dose: 200 mg orally, then 100 mg every 12 hours. *Children <45 kg:* 4.4 mg/kg divided into 2 doses on the first day of treatment followed by maintenance dose of 2.2 mg/kg orally as a single dose or divided dose every 12 hours.

TABLE 40.1 Drug Emphasis Table: Systemic Acne Drugs (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Common adverse effects associated with these treatments include hypersensitivity reactions, yeast infections, and gastrointestinal intolerance. Tetracyclines are also associated with skin rashes, tooth damage and discoloration, and altered bone growth and development. Tetracycline hydrochloride has more specific precautions and contraindications (see Table 40.2) (DailyMed, *Tetracycline Hydrochloride*, 2023).

Table 40.2 is a drug prototype table for systemic acne drugs featuring tetracycline hydrochloride. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Antibiotic (gram-negative and gram-positive) **Mechanism of Action** Bacteriostatic action to reduce bacterial colonization Inhibits protein synthesis	**Drug Dosage** *Oral* *Adults:* 1000 mg daily in divided doses for acute acne; maintenance for acne prevention: 125–500 mg daily. *Children ≥8 years*: 25–50 mg/kg daily, divided into 4 equal doses. *Children <8 years:* Do not administer. *Topical* *3% ointment:* Apply twice daily in a thin layer over the entire affected area.
Indications Acne and other skin infections Sexually transmitted infections (syphilis, chlamydia, gonorrhea) **Therapeutic Effects** Reduces pustules that form in acne by eliminating the bacteria that cause lesions	**Drug Interactions** Antacids Iron Sodium bicarbonate Zinc penicillin Anticoagulants **Food Interactions** Dairy products
Adverse Reactions Gastrointestinal upset Esophageal irritation Enterocolitis Black hairy tongue Yeast infections Tooth discoloration and dental caries Skin rashes that may progress to exfoliative dermatitis Renal and liver toxicities Anemia Thrombocytopenia Neutropenia Severe photosensitivity Anaphylaxis	**Contraindications** Hypersensitivity Children younger than 8 years Pregnancy and lactation Caution: Decreases effectiveness of hormonal contraceptives—barrier contraceptives may be needed

TABLE 40.2 **Drug Prototype Table: Tetracycline Hydrochloride** (source: https://dailymed.nlm.nih.gov/dailymed/)

Topical Acne Drugs

Topical acne medications are often used in combination with systemic acne medications to provide better management of acne. Topical therapy is applied directly to the skin that is affected by the presence of acne lesions. Azelaic acid 15% and benzoyl peroxide 2.5% are used in both acne and rosacea to eliminate bacteria and decrease inflammation as well as to reduce oil on the skin. Salicylic acid, another topical treatment, assists in acne treatment by exfoliating dead skin cells to reduce pore blockages, reducing inflammation, and decreasing sebum secretion. Adapalene 1% topical ointment, when applied to the areas affected by acne, helps to differentiate skin cells and reduces the accumulation of cells in skin pores. Tazarotene, another topical treatment for acne, is thought to assist with reducing fine lines and discolorations in the skin. It is thought that this medication may also play a role in the reduction of scarring from acne lesions. Tretinoin 0.025% ointment, a retinoid, benefits clients undergoing treatment for severe acne. The actions of topical retinoids are not fully understood but are thought to increase cell mitosis and decrease cell cohesion to prevent clogging of skin pores (DailyMed, *Tretinoin,* 2019).

LINK TO LEARNING

The Psychosocial Impact of Skin Disorders (https://openstax.org/r/doiorg10)

Although the physical effects of acne can be devastating, the psychosocial impacts—anxiety/depression, self-

esteem, stigma, body image, social support, social interaction, sexual life, social acceptance and optimism, and objective factors—also must be considered. This NursingOpen article discusses the psychologic impact of acne and other skin disorders (Zhang et al., 2021).

Table 40.3 lists common topical acne drugs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Azelaic acid (Azelex, Finacea, Finevin)	*Adults:* Apply a thin layer topically twice daily. *Children:* Safety and effectiveness have not been established in pediatric clients.
Benzoyl peroxide (Benzac)	*Adults:* Apply a thin layer to the affected area 1–3 times daily. *Children:* Safety and effectiveness have not been established in pediatric clients.
Adapalene (Differin)	*Adults and children ≥12 years:* Apply a thin layer topically once daily, in the evening. *Children <12 years:* Safety and effectiveness have not been established.
Tazarotene (Tazorac)	*Adults:* Apply a thin layer topically once daily, in the evening. *Children:* Safety and efficacy have not been established in clients under the age of 12.
Salicylic acid (Salex, Virasal)	*Adults:* Apply a thin layer topically 1–3 times daily. *Children >2 years:* Follow health care provider recommendations. Not recommended for use in children under 2 years.
Tretinoin (Retin-A, Atralin)	*Adults and children ≥12 years:* Apply a thin layer topically once daily, at night.

TABLE 40.3 **Drug Emphasis Table: Topical Acne Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects for topical acne medications most often involve localized skin redness, scaling, itching, and burning. These may worsen when adapalene is used concomitantly with other substances that cause irritation or dry skin. For this reason, contraindications include the use of other non-approved substances, soaps, and cleansers that cause skin irritation. Other contraindications are sun or other ultraviolent light and the use of occlusive dressings—those that do not allow air or moisture to get in or out.

Table 40.4 is a drug prototype table for topical acne drugs featuring adapalene. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Retinoid, anticomedogenic **Mechanism of Action** Decreases inflammation and clogging of pores in acne	**Drug Dosage** *Adults and children ≥12 years:* Apply a thin layer topically once daily, in the evening. *Children <12 years:* Safety and effectiveness have not been established.
Indications Acne and other skin infections **Therapeutic Effects** Decreases formation of acne lesions	**Drug Interactions** Soaps, creams, and cosmetics that have a drying effect or contain alcohol or astringents **Food Interactions** No significant interactions
Adverse Reactions Skin irritation Redness Itching Flakiness	**Contraindications** Hypersensitivity Dry, flaky, or open skin

TABLE 40.4 **Drug Prototype Table: Adapalene** (source: https://dailymed.nlm.nih.gov/dailymed/)

SPECIAL CONSIDERATIONS

Topical Acne Drugs

Adolescents using topical acne medications are at high risk of discontinuing treatment prematurely because of improved symptoms, side effects, and the need to use multiple products or treatments. Research suggests that monotherapy, treatment with oral medications, and/or anticipatory guidance on side effects can increase an adolescent client's adherence to the prescribed therapy.

(Source: Habeshian & Cohan, 2020)

Nursing Implications

The nurse should do the following for clients who are taking acne drugs:

- Assess and thoroughly document skin condition baseline.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Evaluate and document the client's response to current treatment and overall improvement of skin condition.
- Assess the psychosocial impact of acne on individual clients.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a systemic acne medication should:

- Take prescribed medications exactly as directed.
- Report side effects such as skin redness, excessive dryness, or peeling to their health care provider.
- Use birth control methods as instructed and avoid pregnancy.
- Refrain from breastfeeding.
- Follow up with appointments as instructed.

The client taking a topical acne medication should:

- Take prescribed medications exactly as directed.
- Report side effects such as skin redness, excessive dryness, or peeling to their health care provider.
- Cleanse skin thoroughly before applying medication.
- Apply only a thin layer of medications to the affected areas only.
- Avoid contact with eyes and mucous membranes.
- Wash hands well before and after application.

The client taking a topical acne medication *should not:*

- Cover the medication with occlusive dressings.

FDA BLACK BOX WARNING

Systemic Acne Medications

Embryo-fetal loss and malformations may occur when systemic acne drugs are administered to a pregnant client.

40.3 Psoriatic Drugs

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 40.3.1 Identify the characteristics of drugs used to treat psoriasis.
- 40.3.2 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat psoriasis.
- 40.3.3 Describe nursing implications of drugs used to treat psoriasis.
- 40.3.4 Explain the client education related to drugs used to treat psoriasis.

Psoriasis is a T-lymphocyte–mediated autoimmune disease that mainly affects the skin. In many cases, however, it also affects the eyes, joints, and nails. Plaque psoriasis is the subtype of psoriasis that affects the skin. In this condition, skin cells mature faster than normal, resulting in white-silvery **plaques** on body surfaces with red, erythematous lesions below (see Figure 40.4). The head and scalp, eyes, elbows, knees, and back are primarily affected by these plaques. Plaque psoriasis may range from very mild with few lesions to severe, with large areas of disfiguring plaques. Treatment of psoriasis involves combination systemic and topical therapies used to decrease inflammation, exfoliate skin plaques, and decrease the mitotic rate and maturation of skin cells.

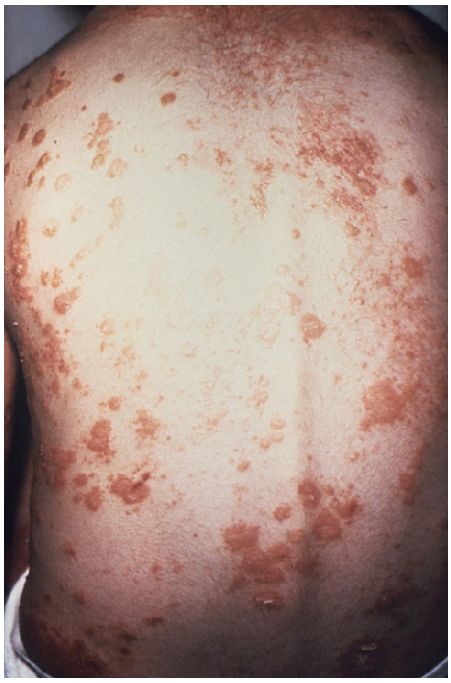


FIGURE 40.4 Psoriatic plaques can be widespread on the body. (credit: "The back of this patient displayed numerous erythematous patches dispersed over the entirety of his back that was diagnosed as a case of psoriasis, an erythematous skin condition characterized by irregular red patches covered by a dry scaly hyperkeratotic stratum corneum."/Centers for Disease Control and Prevention, Public Domain)

Systemic Psoriatic Drugs

Systemic drugs used in the treatment of psoriasis include methoxsalen and acitretin. Methoxsalen is not effective as a monotherapy. It is used in combination with ultraviolet (UV) light therapy to increase its effects. A safety concern with the use of this medication is that when clients are exposed to other sources of UV light, such as the sun, they may experience severe skin burns. Methoxsalen is reserved for treatment of severe psoriasis that has been nonresponsive to other therapies.

Acitretin, a retinoid, may be used alone or in combination with UV therapy or other medications to treat severe, refractory psoriasis. Like other retinoids, acitretin requires very specific monitoring and prescribing limitations, especially with consideration of reproductive health. Prescriptions cannot be given until pregnancy tests and other screenings have been completed and results verified (DailyMed, *Acitretin,* 2023).

Table 40.5 lists common systemic psoriatic drugs and typical routes and dosing for adult clients.

Drug	Routes and Dosage Ranges
Acitretin (Soritane)	25–50 mg orally once daily with main meal.
Methoxsalen (Oxsoralen)	Take 1½ to 2 hours before UVA exposure with some low-fat food or milk according to the following weight guidelines: *<30 kg:* 10 mg. *30–50 kg:* 20 mg. *51–65 kg:* 30 mg. *66–80 kg:* 40 mg. *81–90 kg:* 50 mg. *91–115 kg:* 60 mg. *>115 kg:* 70 mg.

TABLE 40.5 **Drug Emphasis Table: Systemic Psoriatic Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Systemic psoriatic drugs that are classified as retinoids may cause systemic effects such as hypersensitivities, hypervitaminosis A syndrome, myocardial infarction, stroke, thromboembolism, neuropathy, yeast infections, capillary leak syndrome, exfoliative dermatitis, and skin fragility. These drugs are contraindicated in clients with pre-existing cardiac, renal, and hepatic conditions. As mentioned, methoxsalen may cause severe burning of the skin when clients are exposed to UV light. Use in clients receiving UV treatments and who are exposed to the sun may be contraindicated or require dose reductions. Retinoids, such as acitretin, are contraindicated for those who could become pregnant, are pregnant, or are breastfeeding.

Table 40.6 is a drug prototype table for systemic psoriatic drugs featuring acitretin. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Retinoid **Mechanism of Action** Assists in regulating mitotic rate of skin cells	**Drug Dosage** 25–50 mg orally once daily with main meal.
Indications Psoriasis **Therapeutic Effects** Decreases psoriatic plaque formation	**Drug Interactions** Tetracycline drugs Methotrexate **Food Interactions** No significant interactions
Adverse Reactions Hypersensitivity Hypervitaminosis A syndrome Myocardial infarction Stroke Thromboembolism Neuropathy Yeast infections Capillary leak syndrome Exfoliative dermatitis Skin fragility	**Contraindications** Hypersensitivity Liver or kidney disease Hyperlipidemia Pregnancy

TABLE 40.6 **Drug Prototype Table: Acitretin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking systemic psoriatic drugs:

- Ensure that clients have met required screening to receive prescriptions for systemic psoriatic medications.
- Assess and thoroughly document baseline skin condition.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Evaluate and document the client's response to current treatment and overall improvement of skin condition.
- Assess the psychosocial impact of psoriasis on individual clients.
- Provide client teaching regarding the drug and when to call the health care provider. See the end of this section for client teaching guidelines.

Topical Psoriatic Drugs

Topical therapies for treating psoriasis decrease the mitotic rate and differentiation of skin cells in the epidermis. Calcipotriene, a vitamin D analog, blocks vitamin D receptors in the skin to decrease skin cell production. Clobetasol, a topical steroid, reduces inflammation associated with psoriasis. This medication is only used in clients over 12 years of age. Application of clobetasol is limited to those areas that are not on the face, genitals, and axillae. It is important to remember that clients may experience systemic steroidal effects. For this reason, clobetasol should be limited to use for 2 weeks or less.

Coal tar is another topical medication that treats the itching, redness, and scaliness associated with psoriasis. Coal tar, along with anthralin, should not be applied to the skin surrounding the psoriatic lesions. Petrolatum or zinc oxide ointments may be used to coat the normal surrounding tissues before medication administration to protect the normal tissue. Tazarotene, as with treatment for acne, is thought to assist with reducing discolorations in the skin and may also play a role in reduction of scarring from psoriatic lesions.

Table 40.7 lists common topical psoriatic drugs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Clobetasol (Dermovate, ClobaDerm, Etrivex)	*Adults and children ≥12 years:* Apply aerosol foam (0.05%) topically in a thin layer twice daily for 2 weeks.
Calcipotriene	*Adults:* Apply ointment (0.005%) topically, rubbing gently on lesions 1–2 times daily.
Coal tar lotion (Cutar) Coal tar shampoo (Psoriderm, Exorex, Polyderm)	*Adults:* *Lotion (8%):* Apply to affected areas 1–4 times daily. *Shampoo (5%):* Shake well, apply to wet hair, gently massage into hair and scalp to work up a lather. Rinse thoroughly and repeat. Use at least twice a week or as directed.
Tazarotene (Tazorac)	*Adults:* Apply a thin layer topically, once daily in the evening. *Children:* Safety and efficacy have not been established in clients under the age of 18.

TABLE 40.7 Drug Emphasis Table: Topical Psoriatic Drugs (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Topical treatments for psoriasis are contraindicated for areas of open skin, mucous membranes, genitals, and the face. Adverse effects may be related to improper use of these medications. Applying too much or too often may cause excessive drying and irritation of the skin. Redness, flaking, or broken areas may also develop with improper use (DailyMed, *Tazarotene*, 2023).

Table 40.8 is a drug prototype table for systemic psoriatic drugs featuring coal tar. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Psoriatic **Mechanism of Action** Assists in treating redness, scaling, and itching of psoriatic lesions	**Drug Dosage** *Adults:* *Lotion (8%):* Apply to affected areas 1–4 times daily. *Shampoo (5%):* Shake well, apply to wet hair, gently massage into hair and scalp to work up a lather. Rinse thoroughly and repeat. Use at least twice a week or as directed.
Indications Psoriasis **Therapeutic Effects** Decreases itching, redness, and scaling of psoriatic plaques	**Drug Interactions** No significant interactions **Food Interactions** No significant interactions
Adverse Reactions Rash Skin irritation	**Contraindications** Hypersensitivity UV light/sun exposure

TABLE 40.8 **Drug Prototype Table: Coal Tar** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking topical psoriatic drugs:

- Assess and thoroughly document baseline skin condition.
- Observe for hypersensitivity reactions or worsening of symptoms.
- Assess for prolonged use or excessive application by clients.
- Evaluate and document the client's response to current treatment and overall improvement of skin condition.
- Assess the psychosocial impact of psoriasis on individual clients.
- Provide client teaching regarding the drug and when to call the health care provider. See the end of this section for client teaching guidelines.

Biologic Psoriatic Drugs

Biologic response modifiers and monoclonal antibodies are used in the treatment of psoriasis and other autoimmune diseases to reduce inflammation. Etanercept and infliximab decrease inflammation in psoriasis by inhibiting the action of tumor necrosis factor (TNF), substances within the body that stimulate immune responses and produce inflammatory effects. Adalimumab and ustekinumab are monoclonal antibodies that help to decrease inflammation as well but do so by affecting T-cell response through the inhibition of interleukin-12 and interleukin-23.

Table 40.9 lists common biologic psoriatic drugs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Etanercept (Enbrel)	*Adults and children ≥63 kg:* 50 mg subcutaneous injection twice weekly for 3 months, then weekly for maintenance. *Children <63 kg:* 0.8 mg/kg subcutaneous injection weekly.
Infliximab (Remicade)	*Adults:* 5 mg/kg intravenous (IV) infusion on weeks 0, 2, and 6, then every 8 weeks thereafter. *Children:* Safety and efficacy for use in psoriasis have not been established in clients under the age of 17.

TABLE 40.9 **Drug Emphasis Table: Biologic Psoriatic Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Adalimumab (Humira)	*Adults:* Initial dose: 80 mg subcutaneously, then 40 mg every other week. *Children:* Safety and efficacy for use in psoriasis have not been established in clients under the age of 17.
Ustekinumab (Stellara)	*Adults and children >100 kg:* 90 mg subcutaneously initially, then 4 weeks later, then 90 mg every 12 weeks. *Adults and children ≤100 kg:* 45 mg subcutaneously initially, then 4 weeks later, then 45 mg every 12 weeks. *Children <60 kg:* 0.75 mg/kg subcutaneously. Follow the adult administration timeframe but use weight-based guidelines to administer the same dose at each scheduled interval.

TABLE 40.9 **Drug Emphasis Table: Biologic Psoriatic Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

The use of biologic drugs in psoriasis is associated with hypersensitivity reactions to the proteins that comprise these drugs. Because these drugs suppress the immune system to reduce inflammation, they can increase a client's risk for serious, often life-threatening infections. Additionally, the immunosuppressive effects can cause secondary malignancies to develop, especially lymphomas. These medications are contraindicated for those clients who have infections, immunosuppressive conditions, or who may be taking other immunosuppressive treatments.

Table 40.10 is a drug prototype table for biologic psoriatic drugs featuring adalimumab. It lists drug class, mechanism of action, adult dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class TNF blocker, monoclonal antibody **Mechanism of Action** Binds to TNF to block action of tumor necrosis factor–mediated inflammation Decreases scaling of skin	**Drug Dosing** *Adults:* Initial dose: 80 mg subcutaneously, then 40 mg every other week. *Children:* Safety and efficacy for use in psoriasis have not been established in clients under the age of 17.
Indications Plaque psoriasis **Therapeutic Effects** Systemically reduces inflammation associated with plaque psoriasis and other autoimmune diseases	**Drug Interactions** Cytochrome P450 substrates Anticoagulants Cyclosporine Theophylline **Food Interactions** No significant interactions
Adverse Reactions Bacterial infections Yeast infections Neutropenia Anaphylaxis Secondary malignancies Heart failure	**Contraindications** Hypersensitivity Caution: Clients at higher risk of infection

TABLE 40.10 **Drug Prototype Table: Adalimumab** (source: https://dailymed.nlm.nih.gov/dailymed/)

Nursing Implications

The nurse should do the following for clients who are taking biologic psoriatic drugs:

- Conduct vigilant assessments for baseline, response to treatment, adverse effects, infection, and secondary malignancies.
- Evaluate blood urea nitrogen (BUN), creatinine, and glomerular filtration rate for renal function; review liver function tests for hepatotoxicity.

- Ensure client received tuberculosis screening before initiation of therapy.
- Observe for hypersensitivity reactions during and after administration.
- Emphasize the importance of compliance with instructions and follow up with clients when necessary.
- Assess and monitor the client for adverse effects, drug and food interactions, and contraindications.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client taking a systemic psoriatic medication should:

- Take prescribed medications exactly as directed.
- Report side effects such as skin redness, excessive dryness, or peeling to the primary provider.
- Report temperature above 100.4°F, chills, productive cough, and symptoms of urinary tract or other infections immediately.
- Avoid crowds or others who are sick or who have received live vaccines in the last 3 months.
- Use birth control methods as instructed and avoid pregnancy.
- Refrain from breastfeeding.
- Avoid UV light exposure (methoxsalen).
- Follow up with appointments as instructed.

The client taking a topical psoriatic medication should:

- Take prescribed medications exactly as directed.
- Report side effects such as skin redness, excessive dryness, or peeling to the primary provider.
- Cleanse skin thoroughly before applying medication.
- Apply only a thin layer of medications to the affected areas only.
- Avoid contact with eyes and mucous membranes.
- Wash hands well before and after application.

The client taking a topical psoriatic medication *should not*:

- Cover the medication with occlusive dressings.
- Get the medication on clothing or other fabrics because it causes staining.

The client taking a biologic psoriatic medication should:

- Take medications exactly as instructed.
- Follow up with appointments.
- Report temperatures above 100.4°F to their health care provider.
- Contact the primary provider for productive cough, symptoms of urinary tract infection, yeast infection, or other unusual symptoms.
- Continue lifelong follow-ups for monitoring for secondary malignancies.
- Avoid crowds and other exposures to people with infections.
- Avoid contact with those who have had live virus vaccinations within 3 months.

FDA BLACK BOX WARNING

Psoriatic Medications

Acitretin can cause embryo-fetal loss and malformations when administered to a pregnant client.

Methoxsalen can cause severe photosensitivity, ocular damage, skin aging, and skin cancers.

Infliximab, adalimumab, and **ustekinumab** can increase the risk of serious infections and the development of secondary malignancies.

40.4 Other Dermatologic Condition Drugs and Topical Anti-infectives for Burns

LEARNING OUTCOMES

By the end of this section, you should be able to:

- 40.4.1 Identify the characteristics of drugs used to treat miscellaneous dermatologic disorders and burns.
- 40.4.2 Explain the indications, actions, adverse reactions, and interactions of drugs used to treat miscellaneous dermatologic disorders and burns.
- 40.4.3 Describe nursing implications of drugs used to treat miscellaneous dermatologic disorders and burns.
- 40.4.4 Explain the client education related to drugs used to treat miscellaneous dermatologic disorders and burns.

In addition to acne and psoriasis, there are other common skin conditions for which clients may receive treatment. In this chapter they are divided into miscellaneous dermatologic conditions and burns.

Miscellaneous Dermatologic Disorders

This section focuses on the most common dermatological disorders not yet discussed, including cutaneous warts, atopic dermatitis (eczema), contact dermatitis, impetigo, and rosacea.

Cutaneous Warts

Cutaneous warts are a form of localized viral infection, resulting in the familiar raised lesions known as warts (Figure 40.5). Current therapies in the treatment of warts include medications that chemically burn these lesions, thus eliminating them. Cantharidin is one such drug. As a **vesicant**, cantharidin causes local tissue necrosis on those surfaces to which it is applied. This necrosis will eventually result in the sloughing of the wart and elimination of the virus.

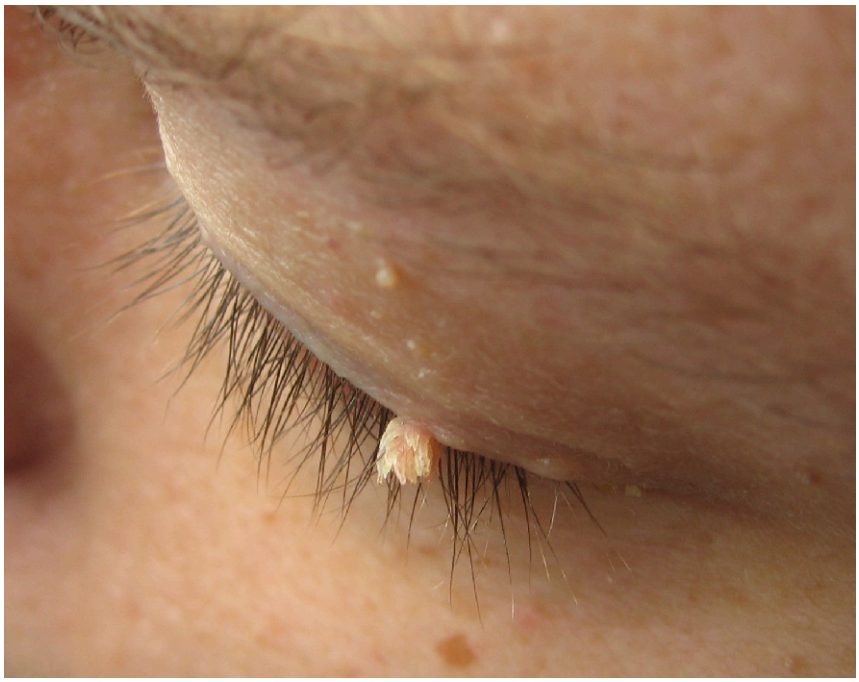


FIGURE 40.5 A cutaneous wart has an irregular shape and surface. (credit: "Filiform wart on the eyelid" by Schweintechnik/Wikimedia Commons, Public Domain)

Atopic Dermatitis (Eczema)

Atopic dermatitis (**eczema**) is another skin condition that requires pharmacological treatment. Unlike conditions characterized solely by local irritation, atopic dermatitis is a systemic disease that has genetic predispositions, involves the immune system, and also has environmental influences. This condition has also been linked to other disorders, including asthma and hay fever (National Institute of Arthritis and Musculoskeletal and Skin Diseases,

2022). The etiology is not clearly understood, but treatment involves using oral and topical medications to relieve the characteristic lesions of atopic dermatitis (Figure 40.6). Hydrocortisone and pimecrolimus are often used topically to treat atopic dermatitis.

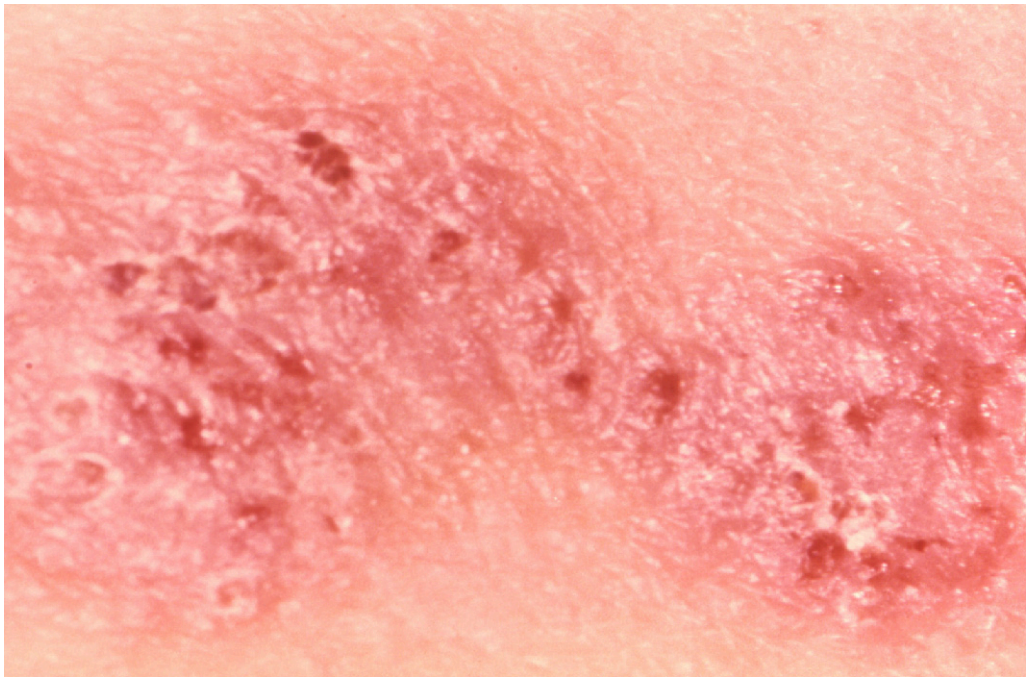


FIGURE 40.6 Atopic dermatitis/eczema characteristically appears as red, dry patches. (credit: "This image depicts a close view of a cutaneous lesion known as nummular eczema, which also goes by the names nummular dermatitis, or discoid eczema, which presents itself as round [PHIL 16526], or oval-shaped erythematous, itchy patches" by Susan Lindsley/Centers for Disease Control and Prevention, Public Domain)

Contact Dermatitis

Contact dermatitis is an acute inflammation caused by aggravating factors that results in swollen, red, itchy lesions (Figure 40.7). Substances that may cause contact dermatitis include, but are not limited to, soaps, cosmetics, jewelry, and poison ivy/oak. Treatment focuses on decreasing inflammation and providing comfort and decreased pain and itching. Hydrocortisone, when applied to areas of contact dermatitis, acts to decrease inflammation, relieving the red, warm, edematous symptoms. In addition to hydrocortisone or other corticosteroid ointments, calamine lotion also may be used to reduce itching and promote healing. This solution is made by combining zinc oxide and ferric oxide, which, when applied to the skin, soothes the affected area and reduces itching and burning at the site.

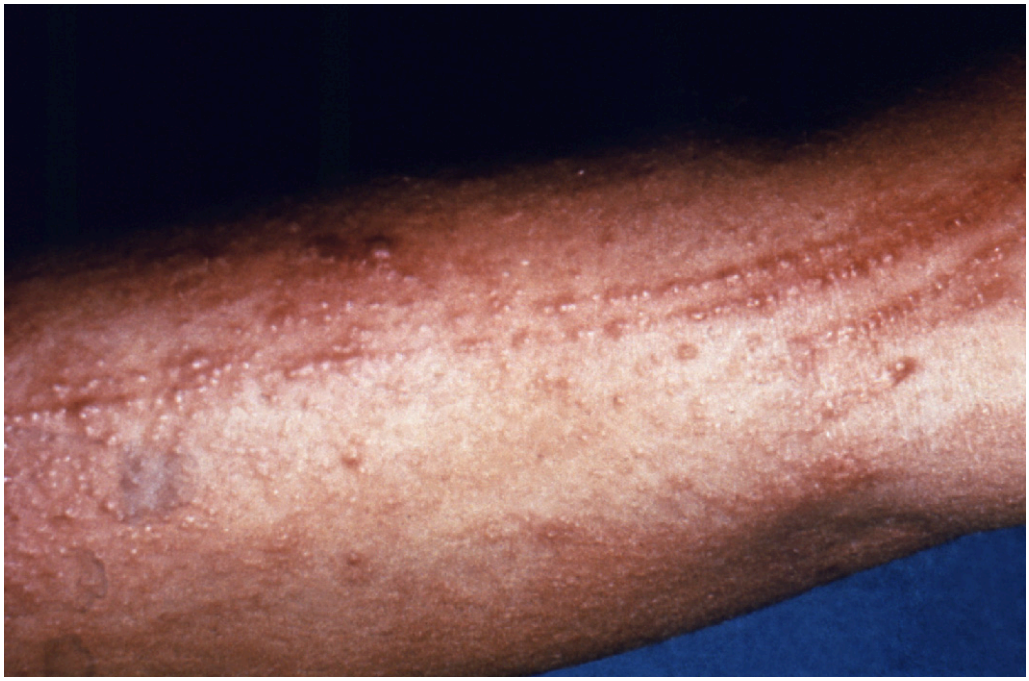


FIGURE 40.7 Contact dermatitis is acute inflammation resulting from direct contact with irritants. (credit: "This photograph depicts an individual's arm with a blistering poison oak rash."/Centers for Disease Control and Prevention, Public Domain)

Impetigo

Impetigo is a cutaneous bacterial infection that occurs on the upper surface of the skin (Figure 40.8). Typically, impetigo is seen in infants and children, although it may occasionally be seen in adults. The causative organisms are most often *Staphylococcus aureus* and *Streptococcus pyogenes* bacteria. Treatment encompasses application of mupirocin, a topical antibacterial. Retapamulin, another topical anti-infective used in impetigo, selectively inhibits protein synthesis to stop bacterial growth. Topical treatment with these agents usually clears impetigo, but if impetigo persists and is severe, oral antibiotics may be needed.

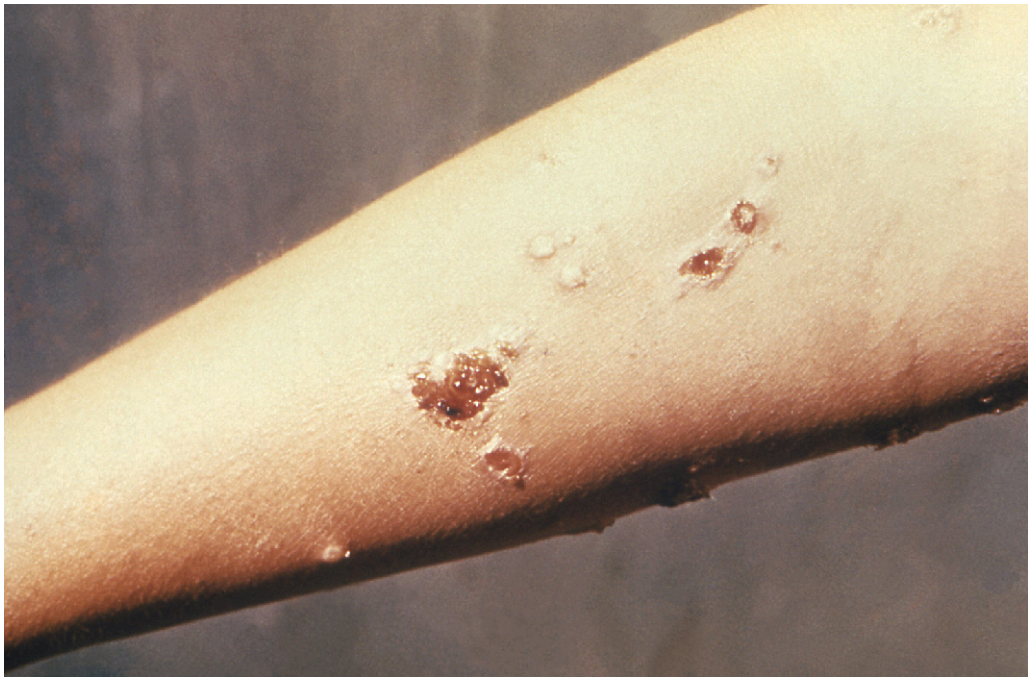


FIGURE 40.8 Impetigo is characterized by vesicles, pustules, or bullae that rupture, producing sores covered by honey-colored crusts. (credit: "The lesions on the volar surface of this patient's left forearm proved to be *Streptococcal* impetigo, a dermatologic condition quite often caused by *Staphylococcus aureus* bacteria, as well" by Dr. Herman Miranda, Univ.of Trujello, Peru; A. Chambers/Centers for Disease Control and Prevention, Public Domain)

Rosacea

Rosacea is a skin condition that develops from an inflammatory process, causing redness, swelling, prominent small vessels, and papular lesions on the face (Figure 40.9). Metronidazole, an antifungal, is used in the treatment of rosacea to reduce redness and inflammatory lesions. Nurses should note that when absorbed systemically, metronidazole interacts negatively with many other medicines. When alcoholic beverages are mixed with metronidazole, a life-threatening disulfiram-like reaction may occur, resulting in palpitations, diaphoresis, flushing, nausea, and tachycardia (Stokes & Abdijadid, 2019). Sodium sulfacetamide, another treatment for rosacea, is antibacterial in function and is used to cleanse the skin and eliminate bacteria. Clients with sulfa allergies should not use sodium sulfacetamide.

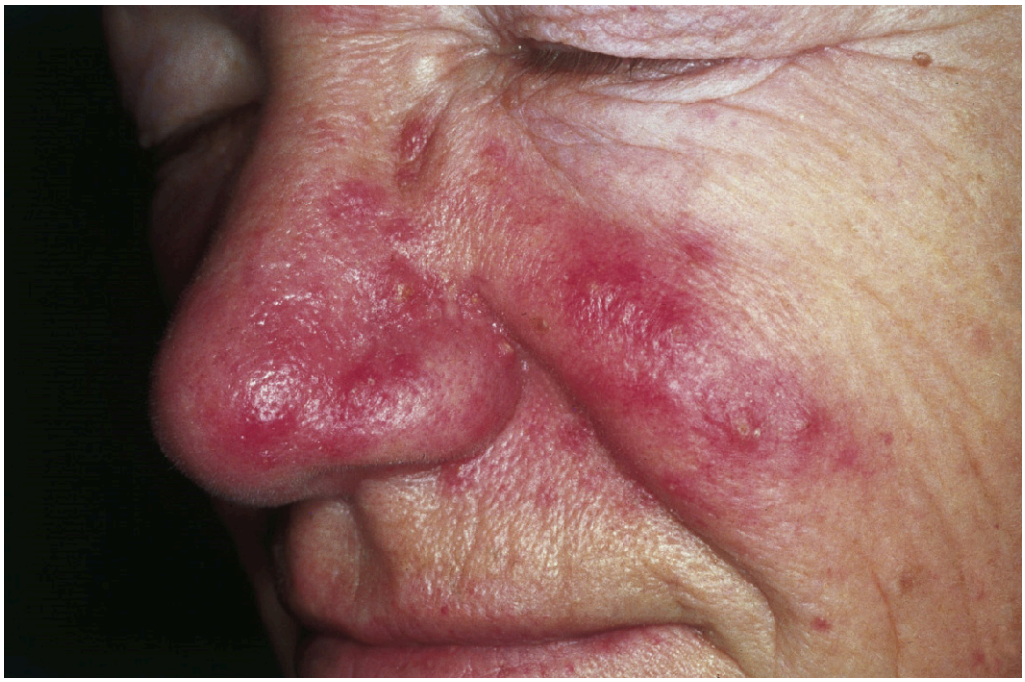


FIGURE 40.9 Rosacea, consisting of red bumps and broken blood vessels, occurs on the face. (credit:"Rosacea. Erythema and telangiectasia are seen over the cheeks, nasolabial area and nose. Inflammatory papules and pustules can be observed over the nose. The absence of comedos is a helpful tool to distinguish rosacea from acne." by Sand, M., Sand, D., Thrandorf, C. et al. "Cutaneous lesions of the nose." *Head Face Med* 6, 7 [2010]. https://doi.org/10.1186/1746-160X-6-7/BioMed Central, CC BY 2.0)

Table 40.11 lists common miscellaneous dermatologic drugs and typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Hydrocortisone (Cortef)	*Adults and children >2 years:* Apply 1% cream topically to affected area 3 times daily.
Methylprednisolone (Medrol)	*Adults:* 4–48 mg/day orally, depending on the specific disease entity being treated.
Calamine lotion (Calananz)	*Adults and children >2 years:* Apply to area as needed, let dry.
Retapamulin (Altabax)	*Adults:* Apply a thin layer to the affected area (not to exceed 100 cm^2) twice daily for 5 days. *Children ≥9 months:* Apply a thin layer on areas not to exceed 2% total body surface area twice daily for 5 days.
Mupirocin (Bactroban)	*Adults and children >2 months:* Apply ointment (2%) to area 2–3 times daily.
Metronidazole (Flagyl)	*Adults:* Apply gel (0.75%) topically and rub in a thin film twice daily, morning and evening. *Children:* Safety and effectiveness in pediatric clients have not been established.

TABLE 40.11 **Drug Emphasis Table: Other Dermatologic Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

Drug	Routes and Dosage Ranges
Sodium sulfacetamide (Sumaxin, Cetamide)	*Adults:* Wash affected areas with 10% gel twice daily (morning and evening) or as directed by your physician. *Children:* Safety and effectiveness in children under 12 years has not been established.
Pimecrolimus (Elidel)	*Adults and children >2 years:* Apply a thin layer of 1% cream to affected areas twice daily.
Cantharidin (Yanth)	*Adults and children >2 years:* Apply topically to wart surface only; repeat every 3 weeks as needed.

TABLE 40.11 **Drug Emphasis Table: Other Dermatologic Drugs** (source: https://dailymed.nlm.nih.gov/dailymed/)

SAFETY ALERT

Topical Steroids

When using topical steroids, the application sites should not be covered with an occlusive dressing. Breathable gauze dressings may be used. Topical corticosteroids are meant to exert a local effect; however, when these medications are covered with an occlusive dressing, systemic absorption may occur, leading to systemic side effects of the drug.

Adverse Effects and Contraindications

Adverse effects associated with topical medications for skin disorders include hypersensitivities. This is especially associated with mupirocin. Localized irritation, redness, and peeling may be noted with these medications as well. When covered with occlusive dressings, clients may experience systemic absorption, resulting in the likelihood of systemic effects. For this reason, occlusive dressings are contraindicated.

Steroid compounds are contraindicated in fungal infections. Long-term use of pimecrolimus, a calcineurin inhibitor, has been associated with the development of lymphomas. For this reason, long-term use is contraindicated.

Table 40.12 is a drug prototype table for common dermatologic medications featuring mupirocin. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Topical antibiotic **Mechanism of Action** Bactericidal; binds RNA transcription	**Drug Dosing** *Adults and children >2 months:* Apply ointment (2%) to area 2–3 times daily.
Indications Impetigo **Therapeutic Effects** Eradication of impetigo lesions	**Drug Interactions** Other topical medications used concurrently **Food Interactions** No significant interactions
Adverse Reactions Atopic dermatitis Contact dermatitis Pruritis Hypersensitivities including anaphylaxis	**Contraindications** Hypersensitivity Caution: Avoid occlusive dressings to prevent systemic absorption

TABLE 40.12 **Drug Prototype Table: Mupirocin** (source: https://dailymed.nlm.nih.gov/dailymed/)

Topical Anti-infectives for Burns

The greatest risk from minor burns is infection. Because a burn removes layers of skin, an open lesion forms, breaking the skin's integrity and allowing bacteria and other organisms to enter the client's body. Silver sulfadiazine

and mafenide acetate are two topical anti-infectives used in the treatment and prevention of infection for localized second- and third-degree burns. As with sodium sulfacetamide, these medications are sulfa compounds that should not be administered to those with sulfa allergies. The nurse should take care to maintain a sterile environment when applying these medications to aid in preventing bacterial transfer to the client. To remain effective, burns should be completely covered with cream at all times to prevent bacterial colonization (DailyMed, *Sulfamylon,* 2023).

Table 40.13 lists common topical medications used in treating burns with typical routes and dosing for adult and pediatric clients.

Drug	Routes and Dosage Ranges
Mafenide acetate (Sulfamylon)	*Adults and children >2 months:* Apply cream once or twice daily, to a thickness of approximately $\frac{1}{16}$ inch.
Silver sulfadiazine (Silvadene)	*Adults and children >2 months:* Apply cream once or twice daily, to a thickness of approximately $\frac{1}{16}$ inch.

TABLE 40.13 Drug Emphasis Table: Topical Anti-infectives for Burns (source: https://dailymed.nlm.nih.gov/dailymed/)

Adverse Effects and Contraindications

Adverse effects associated with topical medications for burns include hypersensitivities, pruritis, localized irritation, redness, and peeling. When covered with occlusive dressings, clients may experience systemic absorption, resulting in the likelihood of systemic effects. For this reason, occlusive dressings are contraindicated. Contraindications include hypersensitivities to drugs or their components.

Table 40.14 is a drug prototype table for common burn treatments featuring silver sulfadiazine. It lists drug class, mechanism of action, adult and pediatric dosage, indications, therapeutic effects, drug and food interactions, adverse effects, and contraindications.

Drug Class Topical antibiotic **Mechanism of Action** Bactericidal; disrupts cell wall	**Drug Dosing** *Adults and children >2 months:* Apply cream once or twice daily, to a thickness of approximately $\frac{1}{16}$ inch.
Indications Second- and third-degree burns **Therapeutic Effects** Absence of infectious organisms in wound bed	**Drug Interactions** Other topical medications used concurrently Cimetidine **Food Interactions** No significant interactions
Adverse Reactions Hypersensitivities Necrosis Erythema multiforme Skin discoloration Burning sensation Rashes Interstitial nephritis Leucopenia	**Contraindications** Hypersensitivity Sulfa allergy Pregnant clients approaching or at term Premature infants or newborn infants during the first 2 months of life

TABLE 40.14 Drug Prototype Table: Silver Sulfadiazine (source: https://dailymed.nlm.nih.gov/dailymed/)

! SAFETY ALERT

Silver Sulfadiazine

Silver sulfadiazine is widely used for burns with low risk of adverse effects. Overdose is uncommon, but systemic

absorption can still occur. Care should be taken when applying the medication near mucosal or ocular areas or when it is used over a large body surface area.

(Source: Oaks & Cindass, 2023)

Nursing Implications

The nurse should do the following for clients who are using drugs for the treatment of burns:

- Conduct vigilant assessments for baseline, response to treatment, adverse effects, infection, and systemic absorption.
- Monitor creatinine for decreased renal function from possible effects of systemic absorption.
- Observe for hypersensitivity reactions during and after administration.
- Apply topical medications with gloves.
- Maintain aseptic technique when applying medications.
- Emphasize the importance of compliance with instructions and follow up with clients when necessary.
- Provide client teaching regarding the drug and when to call the health care provider. See below for client teaching guidelines.

CLIENT TEACHING GUIDELINES

The client using a topical medication for burns should:

- Take prescribed medications exactly as directed.
- Wash hands well before and after application.
- Report side effects such as skin redness, excessive dryness, or peeling to the primary provider.
- Report drainage, odor, temperature above 100.4°F, or other unusual symptoms to the primary provider.
- Cleanse skin thoroughly before applying medication.
- Avoid contact with eyes and mucous membranes.

The client using a topical medication for burns *should not:*

- Cover the medication with occlusive dressings.

FDA BLACK BOX WARNING

Pimecrolimus

Pimecrolimus cream has been associated with skin malignancies and lymphoma. Continuous long-term use should be avoided in any age group. Its use is not indicated for children less than 2 years of age.

CASE STUDY

Read the following clinical scenario to answer the questions that follow.

Within the last year, Melissa Allen, a 27-year old patient, has gotten married, moved to a new city, and begun graduate school. Recently, she has noticed feeling a little more tired than usual and has experienced generalized joint pain.

History
Right ankle fracture
Seasonal sinusitis

Current Medications

Ibuprofen, 400 mg every 4 hours as needed
Yasmin birth control pill (drospirenone 3 mg/ethinyl estradiol 0.03 mg)

Vital Signs		Physical Examination
Temperature:	97.4°F	• *Head, eyes, ears, nose, throat (HEENT):* Denies any changes in vision; responds to questions appropriately without requests for repeats • *Neurological:* Alert and oriented × 4, pleasant affect; denies numbness, tingling, dizziness, or headache • *Cardiovascular:* Regular heart rate and rhythm; denies palpitations; S1, S2 audible; no extra sounds noted; capillary refill +3; mucous membranes pink, moist, and intact • *Respiratory:* Lungs clear to auscultation in all fields; denies shortness of breath • *GI:* Abdomen soft, nontender, without distention; bowel sounds active in all quadrants; denies nausea, vomiting, diarrhea, or constipation • *GU:* Last menstrual period 16 days ago • *Integumentary:* Nails with cracking noted; scalp with excessive silvery scaling and reddened areas noted; skin intact to limbs and trunk except for small scaling; red areas noted bilaterally on elbows; client states she has noticed more "itching and dandruff" lately
Blood pressure:	126/64 mm Hg	
Heart rate:	88 beats/min	
Respiratory rate:	14 breaths/min	
Oxygen saturation:	100% on room air	
Pain:	3/10	
Height:	5'5"	
Weight:	144 lb	

TABLE 40.15

1. Based on Melissa's subjective and objective assessment data, what diagnosis should the nurse anticipate from the health care provider?
   a. Acne vulgaris
   b. Psoriasis
   c. Impetigo
   d. Rosacea

2. The health care provider prescribes topical coal tar. Which statement by Melissa indicates a need for further teaching from the nurse regarding the use of topical coal tar?
   a. "I guess this means that I will need to cancel my tanning bed membership."
   b. "I should cover the surrounding margins of lesions with a thick coat of medication."
   c. "I will wash my skin, apply the medication, and leave it open to the air."
   d. "I will refrain from using the medication on my face, especially near my eyes."

Chapter Summary

This chapter has presented the pharmacological management of selected skin conditions: acne, psoriasis, atopic dermatitis, contact dermatitis, impetigo, rosacea, and burns. A brief introduction to each condition, specific drug treatments, routes, dosages, adverse effects, nursing interventions, and client teaching have been discussed. Additionally, a special focus on disparities in the diagnosis and treatment of skin conditions and the psychological implications of skin disorders has been included.

Key Terms

acne vulgaris a skin condition in which skin pores and hair follicles become blocked, resulting in inflamed skin lesions

atopic dermatitis (eczema) a long-term, systemic inflammatory response mediated by both genetic and environmental factors expressed as patchy, red, inflamed lesions

contact dermatitis an acute inflammatory skin reaction to an aggravating factor resulting in local redness, itching, and fluid-filled vesicles

cutaneous warts bumps on the skin surface that result from a viral infection

dermis the innermost layer of the skin, composed of two sublayers, found between the epidermis and hypodermis

epidermis the outermost layer of the skin, composed of five sublayers; rests above the dermis

hypodermis the foundation of the skin that anchors the dermis to muscles

impetigo a cutaneous bacterial infection that develops as a honey-colored crust on the skin surface

Langerhans cells cells located within the epidermis that act against invading organisms

papillae fingerlike projections that extend from the dermis into the epidermis and hold the two layers together

plaque a raised, well-demarcated skin lesion arising from damage or deposits on the skin

psoriasis a systemic condition of the skin resulting from increased skin cell mitosis

rosacea a reddened facial rash characterized by broken blood vessels and small red bumps

sebum an oily, lipid-based substance that lubricates the skin and hair

superficial fascia the foundation of the skin that anchors the dermis to the muscles

vesicant any IV drug capable of causing blistering and tissue damage if leakage around the IV site occurs

Review Questions

1. The nurse is conducting a follow-up visit with a client who is being treated for psoriasis with adalimumab. Which finding demonstrates a therapeutic response has occurred?

a. Negative wound cultures
b. Decreased neutrophils
c. Decreased scaling
d. Absence of drainage

2. A 32-year-old client diagnosed with acne has been prescribed tretinoin. Which teaching point should the nurse include in the client's discharge instructions?

a. It is essential that you avoid pregnancy throughout therapy with tretinoin.
b. This medication should be used liberally across the affected area four times daily.
c. You may take this medication only during the first 12 weeks of pregnancy.
d. You should stop taking your birth control because it reacts negatively with tretinoin.

3. For which client would the nurse question an order for tetracycline hydrochloride?

a. A 48-year-old client with a history of frequent UTIs
b. A 16-year-old client with severe acne
c. A 6-year-old client diagnosed with impetigo
d. An 86-year-old client undergoing treatment for an infected sebaceous cyst

4. A client newly diagnosed with plaque psoriasis asks the nurse how this condition will be treated. Which is the correct response by the nurse?

a. "You will need surgical intervention to remove these lesions."
b. "Combination therapy to exfoliate and reduce cell maturation will be used."
c. "A steroidal cream should clear this condition in 2 weeks."
d. "You will be given an antibiotic to eliminate bacterial organisms."

5. Which statement, when made by a client, demonstrates that further teaching by the nurse is necessary regarding the use of topical corticosteroids?
a. "I will cover the lesion with an occlusive dressing after I apply the steroid cream."
b. "I should use a thin layer of this medication directly on the lesion."
c. "This medication will reduce irritation and swelling."
d. "I should cleanse my skin before applying this medication."

6. A nursing student asks the nurse how impetigo treatment works. The nurse explains that the primary goal in the treatment of impetigo is to:
a. Reduce swelling and scaling
b. Decrease scarring as the lesion heals
c. Soften the tissues to reduce pain
d. Eliminate the causative bacteria

7. For which client would a nurse question an order for acitretin?
a. A 48-year-old client with a history of renal failure
b. A 32-year-old client with a documented sulfa allergy
c. A 52-year-old client with a diagnosis of osteoarthritis
d. A 68-year-old client with a serum hemoglobin of 10.5 g/L

8. The nurse is applying silver sulfadiazine to burns on a client's arm. The client asks that the nurse cover the area with a dressing to protect it and keep the medication from getting on their clothes. What is the best response by the nurse?
a. "I will apply a gauze dressing, which will protect the area but still allow air to pass through it."
b. "I will apply an occlusive dressing to keep the keep the area sterile."
c. "I will apply an occlusive dressing to ensure the medication is fully absorbed."
d. "It is best to not apply a dressing and leave this open to the air."

9. Upon entering the examination room, the nurse finds a 15-year-old client in tears. The client states, "This acne has ruined my life. No one will ever want to date me with this awful stuff on my face." Which of the following statements by the nurse is most appropriate?
a. "You can manage this with lifelong medications."
b. "I think you should see a psychologist to talk about this."
c. "With proper hygiene and medications, you can manage your acne well."
d. "You must avoid cosmetics and lotions so that your acne will go away."

10. The nurse is preparing to discharge a client with a new prescription for metronidazole. Which statement should be included in the discharge teaching?
a. "Limit your oral fluid intake to 2000 mL/day."
b. "You may stop taking this medication when your skin looks better."
c. "You will experience severe side effects if you drink alcohol while on this drug."
d. "This medication will eliminate the bacterial organisms on your skin."

APPENDIX A

International System of Units

The International System of Units (abbreviated SI for *Système Internationale*) is a system of units of measurement that was established in 1960 and consists of base units and derived units of measurement. This system, more commonly known as the metric system, is periodically updated and maintained by the General Conference on Weights and Measures (GCWM).

The SI system is the most widely used measurement system internationally; however, the United States has not fully adopted the system. It continues to use the U.S. customary system of measurement, except in health care. The common base units and derived units include body mass index, length, mass, temperature, and volume. Table A1 shows the common units derived from the SI and used in health care. Table A2 shows the common prefixes for this system.

For additional information on the SI system, refer to the National Institute of Standards and Technology (NIST) (https://openstax.org/r/nistgovpml) website.

Measurement	Name	Symbol
Body mass index	Kilogram per meter squared	kg/m^2
Length	Meter	m
Mass	Gram	g
Temperature	Degrees Celsius	°C
Volume	Liter	L

TABLE A1 Common SI Units (source: https://www.nist.gov/pml/owm/metric-si/si-units)

Whole Units				Decimal Units		
Thousands	Hundreds	Tens	SI Unit	Tenths	Hundredths	Thousandths
1000	100	10	1	0.1	0.01	0.001
Kilo–	Hecto–	Deka–	Meter Gram Liter	Deci–	Centi–	Milli–

TABLE A2 Common SI Prefixes (source: https://www.nist.gov/pml/owm/metric-si-prefixes)

APPENDIX B

Common Abbreviations and Lab Values

Nurses are required to review and interpret lab values. Table B1 lists common abbreviations, and Table B2 lists common lab values for nurses to learn.

Abbreviation	Meaning	Abbreviation	Meaning
cells/mcL or cells/μL	Cells per microliter	mg/dL	Milligrams per deciliter
cells/mL	Cells per milliliter (cubic centimeter)	microunits/mL	Microunits per milliliter
cm	Centimeter	mL	Milliliter
fl oz	Fluid ounce	mL/minute	Milliliters per minute
fL	Femtoliter	mm	Millimeter
g	Gram	mm^3	Cubic millimeter
g/dL	Grams per deciliter	mm Hg	Millimeters of mercury
HPF	High-power field	mmol/L	Millimoles per liter
IU	International unit	ng/mL	Nanograms per milliliter
kg	Kilogram	oz	Ounce
L	Liter	pg/mL	Picograms per milliliter
lb or #	Pound	Tbsp	Tablespoon
mcg/dL or μg/dL	Micrograms per deciliter	tsp	Teaspoon
mEq/L	Milliequivalents per liter	units/L	Units per liter
mg	Milligram		

TABLE B1 Common Abbreviations

Note that the abbreviation for "micro" is sometimes shown as the Greek mu (μ, as in μL); however, that practice is considered to be error prone by the Institute for Safe Medication Practices and has been supplanted by "mc," as in "mcg" for microgram or "mcL" for microliter.

Arterial Blood Gases							
Base excess/ base deficit	−2 to +2 mEq/L		HCO_3	22–26 mEq/L		$PaCO_2$	35–45 mm Hg
PaO_2	75–100 mm Hg		pH	7.35–7.45		SaO_2	95%–100%
Serum Blood Tests							
Albumin	3.5–5.5 g/dL		Glucose (fasting)	70–99 mg/dL		MCV	80–98 fL
Alk phos	30–120 units/L		Glucose tolerance test	(Start) 70–100 mg/dL (1 hour) <180 mg/dL (2 hours) <140 mg/dL		Monocytes	4000–11,000 cells/mcL
ALT	10–40 units/L					Neutrophils	2000–8250 cells/mcL
Ammonia	40–70 mcg/dL					Phosphorus	3.0–4.5 mg/dL

TABLE B2 Common Lab Values (sources: https://www.abim.org/Media/bfijryql/laboratory-reference-ranges.pdf; https://www.ncbi.nlm.nih.gov/books/NBK536919/; https://my.clevelandclinic.org/health/diagnostics/4053-complete-blood-count; https://emedicine.medscape.com/article/2074001-overview; https://www.ncbi.nlm.nih.gov/books/NBK557685/; https://www.ncbi.nlm.nih.gov/books/NBK532915/)

Amylase	3–125 units/L					Platelet count	150–450 × 10^9/L
AST	10–40 units/L		HDL	(F) >50 mg/dL (M) >40 mg/dL		Potassium	3.5–5.0 mEq/L
Bicarb (HCO_3)	23–28 mEq/L		Hematocrit	(F) 37%–47% (M) 42%–50%		Protein	5.5–9.0 g/dL
Bilirubin, total	0.3–1.0 mg/dL					PT PTT	11–13 seconds 25–35 seconds
BNP	0–100 pg/mL		Hemoglobin	(F) 12–16 g/dL (M) 14–18 g/ dL		RBC	(F) 4.2–5.4 million/mm^3 (M) 4.7–6.1 million/mm^3
BUN	8–20 mg/dL						
Calcium	8.6–10.2 mg/ dL		HgbA1c	4.0%–5.6%		RDW	9.0%–14.5%
Chloride	98–106 mEq/L		INR	0.8–1.2 seconds		SaO_2	95%–100%
Cholesterol	<200 mg/dL		Iron	50–150 mcg/ dL		Sodium	136–145 mEq/L
CK	(F) 30–135 units/L (M) 55–170 units/L		Lactic acid	(Art) <0.6 mmol/L (Ven) 0.7–1.8 mmol/L		Triglycerides (fasting)	<150 mg/dL
CO_2 (CMP)	23–30 mEq/L		LDL	<130 mg/dL		Troponin T	0–0.01 ng/mL
Creatinine	(F) 0.5–1.10 mg/dL (M) 0.70–1.30 mg/ dL		Lipase	10–140 units/L		TSH	0.4–6 mcg/mL
D-dimer	<0.5 mcg/mL		Lymphocytes	20–40 × 10^9/L		WBC	5000–10,000/ mL
GFR	≥90 mL/minute		Magnesium	1.6–2.6 mEq/L			
Miscellaneous Tests							
Fungal (yeast) culture	Negative						
Sputum culture	Negative						
Urine Tests							
Bacteria	Negative		Color	Yellow–amber		pH	4.5–8.0
Bilirubin	Negative		Glucose	Negative		Protein	≤150 mg/dL
Blood	Negative		Ketones	Negative		Specific gravity	1.002
Casts	0–5 HPF		Leukocytes	Negative		WBC	0–5 HPF
Clarity	Clear		Nitrates	Negative		Yeast	Negative

TABLE B2 **Common Lab Values** (sources: https://www.abim.org/Media/bfijryql/laboratory-reference-ranges.pdf; https://www.ncbi.nlm.nih.gov/books/NBK536919/; https://my.clevelandclinic.org/health/diagnostics/4053-complete-blood-count; https://emedicine.medscape.com/article/2074001-overview; https://www.ncbi.nlm.nih.gov/books/NBK557685/; https://www.ncbi.nlm.nih.gov/books/NBK532915/)

Note: The reference values provided in these tables should be used as guidelines only,as they can vary by testing laboratory, instrument type, and demographics of the healthy client population used for comparison. Always use

your facility's lab value guidelines for interpretation or testing. In the Next Generation NCLEX exams, assessment items that contain a numeric laboratory value will include the corresponding normal reference range. See NCLEX FAQs (https://openstax.org/r/healthharvaed).

APPENDIX C

Drug Conversion Tables

Drug conversion tables are utilized with dosage calculations to ensure an appropriate dosage of a drug is being administered to the client as ordered. The metric system is used for prescribing medications, but at times nurses may need to explain medication dosages to clients using household measurements.

Table C1 shows common metric and U.S. customary units of measurement used in health Table C2 shows household equivalents. Drug Administration and the Nursing Process discusses conversion in more detail.

Weight	1 kilogram (kg) 1 gram (g) 1 milligram (mg)	1000 grams (g) 1000 milligrams (mg) 1000 micrograms (mcg or µg)	2.2 pounds (lb or #) 0.035274 ounces (oz)
Volume	1 liter (L)	1000 milliliters (mL)	4.22675 cups
Length	1 kilometer (km) 1 meter (m) 1 centimeter (cm) 2.54 centimeters (cm)	1000 meters (m) 100 centimeters (cm) 10 millimeters (mm) 25.4 millimeters (mm)	3281 feet (ft) 3.281 feet (ft) 0.393 inches (in.) 1 inch (in.)

TABLE C1 Common Metric and U.S. Customary Units of Measurement (sources: https://www.math-salamanders.com/metric-to-standard-conversion-chart.html; https://www.unitconverters.net/volume/liters-to-cups.htm; https://www.nist.gov/pml/owm/approximate-conversions-metric-us-customary-measures; https://www.nist.gov/pml/owm/approximate-conversions-us-customary-measures-metric)

Volume	1 cup	8 fluid ounces (fl oz)	236.6 milliliters (mL)
		1 fluid ounce (fl oz)	29.57 milliliters (mL)
	1 tablespoon (Tbsp)	3 teaspoons (tsp)	14.79 milliliters (mL)
	1 teaspoon (tsp)		4.93 milliliters (mL)

TABLE C2 Household Equivalents (sources: https://www.math-salamanders.com/metric-to-standard-conversion-chart.html; https://www.unitconverters.net/volume/liters-to-cups.htm; https://www.nist.gov/pml/owm/approximate-conversions-metric-us-customary-measures; https://www.nist.gov/pml/owm/approximate-conversions-us-customary-measures-metric)

ANSWER KEY

Chapter 1

Case Study

1. b. The client is well above the recommended 4 grams/day dose based on the manufacturer's recommendation for acetaminophen. Taking the drug every 4 hours equates to taking the drug six times/day ($6 \times 1000 \text{ mg} = 6 \text{ grams/day}$). Taking more than 4 grams of acetaminophen in 24 hours can cause acute liver problems. Educating the client about the importance of safe dosing guidelines can prevent future problems.
2. c. Visits to health care providers may be reduced when clients self-medicate, following the directions that come with the medication, for minor ailments.

Review Questions

1. d. Acetaminophen is the generic form of the drug Tylenol, and they have the same active ingredients. Either formulation would be acceptable.
2. b. Both drugs belong under Schedule II and are highly addictive.
3. b. Ibuprofen is the generic name for Motrin; Motrin is the brand or trade name for ibuprofen. The chemical name for ibuprofen is 2-(4-isobutylphenyl) propanoic acid.
4. a. Generic drugs have the same active ingredients but may have different inactive ingredients.
5. d. Decreased GI motility causes increased transit time in the gut, which increases the time for absorption of the drug. Toxicity may result.
6. c. Toxicity is the greatest concern in this older client who is also underweight. Therefore, this client may require a lower dose of the drug.
7. b. IP collaboration has many advantages, including decreased hospitalization costs, improved client safety, and improved communication regarding team goals.
8. a. The FDA is the regulatory agency tasked with the responsibility of ensuring that all drugs are safe and effective for all individuals across the lifespan.
9. b. Phase II incorporates a relatively small number of volunteers with the disease the drug is designed to treat.
10. b. The first action by the nurse should be to assess the client's medication history and whether or not the client is taking the medications as prescribed. All other actions will be performed, but the assessment should be completed first.

Chapter 2

Review Questions

1. c. The amount of the drug would halve every 4 hours. In 4 hours, 400 mg of the drug would be available. In 8 hours, 200 mg would be available, and in 12 hours, 100 mg of the drug would be available
2. d. The serum creatinine level is an indicator of kidney function.
3. a. An intramuscular injection in the deltoid muscle is administered approximately 1.5 inches below the acromion process in the upside-down triangle formed by the acromion process and the axilla.
4. c. The old patch should be removed before applying a new one to avoid a drug overdose.
5. a. The nurse should insert the needle at a 90-degree angle when administering enoxaparin.
6. b. Drugs are excreted through the kidneys, so drug toxicity can develop in the client with renal insufficiency as drug levels rise because they are not properly eliminated from the body.
7. d. A narrow therapeutic index indicates that it has a narrow safety margin, thus requiring frequent monitoring for drug toxicity.
8. c. Because a portion of an oral dose of a medication is inactivated by the first-pass effect in the liver, a drug that has been administered IV may now require a larger oral dose to achieve a therapeutic effect.
9. d. The best course of action is to request the pharmacy to send up a liquid form of the medicine because that

does not change the route. A caplet that is not scored should not be split by the nurse.

10. b. IV is the fastest route because the medication is 100% bioavailable and has immediate onset.

11. d. The nurse determines that 0.5 mg is equal to 500 mcg and sets up the following equation: $D \div H \times Q = A$. D represents the desired dose (the dose ordered), H the amount on hand or available, Q the quantity or volume of the drug form (tablet, capsule, liquid), and A the amount calculated to be administered to the client. Therefore, $500 \text{ mcg} \div 125 \text{ mcg} \times 1 \text{ tablet} = 4 \text{ tablets}$.

12. b. The nurse sets up the following equation: $D \div H \times Q = A$. D represents the desired dose (the dose ordered), H the amount on hand or available, Q the quantity or volume of the drug form (tablet, capsule, liquid), and A the amount calculated to be administered to the client. Therefore, $150 \text{ mg} \div 100 \text{ mg} \times 1 \text{ mL} = 1.5 \text{ mL}$.

13. a. The nurse sets up the following equation: $D \div H \times Q = A$. D represents the desired dose (the dose ordered), H the amount on hand or available, Q the quantity or volume of the drug form (tablet, capsule, liquid), and A the amount calculated to be administered to the client. Therefore, $4000 \text{ units} \div 5000 \text{ units} \times 1 \text{ mL} = 0.8 \text{ mL}$.

14. a. When converting metric and household units, 4.93 mL (which rounds to 5 mL) is equal to 1 teaspoon; 2 teaspoons are equivalent to 10 mL.

15. c. First, convert the client's weight from pounds to kilograms ($2.2 \text{ lb} = 1 \text{ kg}$ therefore, the client weighs 80 kg). Next, calculate the amount of drug the client should receive: $1.5 \text{ mg/kg} \times 80 \text{ kg} = 120 \text{ mg}$.

16. b. The nurse sets up the following equation: $D \div H \times Q = A$. D represents the desired dose (the dose ordered), H the amount on hand or available, Q the quantity or volume of the drug form (tablet, capsule, liquid), and A the amount calculated to be administered to the client. Therefore, $6 \text{ mg} \div 120 \text{ mg} \times 30 \text{ mL} = 1.5 \text{ mL}$.

17. d. The nurse sets up the following equation: $D \div H \times Q = A$. D represents the desired dose (the dose ordered), H the amount on hand or available, Q the quantity or volume of the drug form (tablet, capsule, liquid), and A the amount calculated to be administered to the client. Therefore, $1250 \text{ units/hour} \div 25{,}000 \text{ units} \times 500 \text{ mL} = 25 \text{ mL/hour}$.

18. a. The nurse sets up the following equation: $D \div H \times Q = A$. D represents the desired dose (the dose ordered), H the amount on hand or available, Q the quantity or volume of the drug form (tablet, capsule, liquid), and A the amount calculated to be administered to the client. Therefore, $60 \text{ mg} \div 20 \text{ mg} \times 5 \text{ mL} = 15 \text{ mL}$.

19. c. The nurse sets up the following equation: $D \div H \times Q = A$. D represents the desired dose (the dose ordered), H the amount on hand or available, Q the quantity or volume of the drug form (tablet, capsule, liquid), and A the amount calculated to be administered to the client. Therefore, $400 \text{ mg} \div 400 \text{ mg} \times 250 \text{ mL} = 250 \text{ mL}$ to be infused over 1 hour.

20. c. First, convert the client's weight from pounds to kilograms ($2.2 \text{ lb} = 1 \text{ kg}$). Therefore, the client weighs 60 kg.
Set the equation up in dimensional analysis:
$$\frac{5 \text{ mcg}}{\text{kg/min}} \times 60 \text{ kg} \times \frac{60 \text{ min}}{1 \text{ hour}} \times \frac{1 \text{ mg}}{1000 \text{ mcg}} \times \frac{250 \text{ mL}}{250 \text{ mg}} = \frac{4{,}500{,}000}{250{,}000} = 18 \text{ mL/hour}.$$

Chapter 3

Review Questions

1. c. HIPAA set forth standards to protect sensitive health information from being disclosed without the consent or knowledge of the individual.

2. d. Beneficence is the ethical principle that requires a nurse to "do good" and to act in ways that promote the health and well-being of their clients.

3. c. Autonomy means having the right to make one's own health care decisions.

4. a. Potential benefits of autonomy include improved outcomes, safety, decreased costs, improved self-confidence, and improved adherence to the care plan.

5. b. The nurse should own the duty of caring for self. This, in turn, will improve client safety when allowing oneself the self-care of time off.

6. c. An adverse drug reaction is an undesired effect that occurs at normal doses of the drug.

7. d. An adverse drug event is client harm resulting from exposure to a drug. This is injury from a medication, a

missed medication, or an inappropriately dosed medication.

8. c. CPOE is the acronym for computerized prescriber order entry, also known as e-prescriber.
9. a. Alerts (both soft alerts and hard alerts) are there to improve client safety.
10. b. The correct order has a leading zero before the decimal point. A trailing zero should not be used.

Chapter 4

Review Questions

1. b. Homeostasis involves maintaining the body's internal temperature despite a rise in the environmental temperature.
2. a. Hyperosmolality occurs when there is a high concentration of solutes in a solution, such as occurs with dehydration.
3. d. Transcellular fluid is the fluid contained within the pleural cavity, separated from the intracellular and extracellular fluid compartments and characterized by limited communication with the rest of the body.
4. d. Chloride and phosphorus are major anions in the extracellular fluid volume. When the client loses extracellular fluid through diarrhea, chloride is lost. The other options listed are cations in the extracellular fluid.
5. b. The intravascular compartment contains plasma and blood.
6. b. Positive feedback in labor involves the release of oxytocin, which stimulates uterine contractions.
7. b. The sodium–potassium ATPase pump moves sodium ions out of the cell and potassium ions into the cell, using energy from ATP activity. This process is necessary for maintaining the normal concentration of electrolytes inside and outside the cell and for normal cellular function.
8. d. Negative feedback helps the body maintain its internal balance. Examples include thermoregulation and regulation of blood glucose levels.
9. a. Approximately 40% of the body's fluid is distributed within the cells (ICF), and the remaining 20% is distributed in the ECF.
10. b. Osmotic equilibrium is the state in which the concentration of solutes is equal on both sides of a semipermeable membrane and there is no net movement of water across the membrane.

Chapter 5

Review Questions

1. b. Convert 1 L to 1000 mL, and then calculate drops needed: $1000 \text{ mL} \times 10 \text{ drops/mL} = 10,000 \text{ drops}$. Then divide the total number of drops by the total number of minutes: $10,000 \text{ drops} \div (6 \text{ hours} \times 60 \text{ minutes/hour}) = 27.78 \text{ drops/minute}$. Round to 28 drops/minute.
2. c. Vitamin C is a water-soluble vitamin that is important for the synthesis of collagen and wound healing.
3. b. Diuretic drugs are prescribed to help the body eliminate excess fluid.
4. c. Itching, hives, and shortness of breath are common symptoms of an allergic reaction to blood or blood products.
5. a. $750 \text{ mL} \div \text{by } 8 \text{ hours} = 93.75 \text{ mL/hour}$. Round to 94 mL/hour.
6. d. Vitamin A is a fat-soluble vitamin that can accumulate in the body and potentially cause toxicity.
7. b. Symptoms of fluid volume deficit include thirst, dry mouth, and tachycardia.
8. d. Iron should be administered 1 to 2 hours before or after calcium because it may alter its effectiveness.
9. b. Echinacea is hepatotoxic; therefore, liver function should be monitored.
10. d. St. John's wort may interact with many other drugs, including antidepressants.

Chapter 6

Review Questions

1. d. Cell-mediated immunity is primarily responsible for recognizing and attacking infected cells, including viral cells.
2. c. When treating RA, hydroxychloroquine is used to modify the disease progression by reducing joint inflammation and preventing joint damage.

3. a. Biologic drugs, particularly tumor necrosis factor-alpha (TNF-alpha) inhibitors, can increase the risk of reactivating latent tuberculosis.
4. c. The five cardinal signs of inflammation are redness (rubor), swelling (tumor), warmth (calor), pain (dolor), and loss of function (functio laesa).
5. c. $800 \text{ mg} \div 200 \text{ mg} = 4 \text{ tablets}$
6. d. A vaccine is a medication containing weakened or killed pathogens or antigens, given to prevent future infections, while an immunization is the process of administering a vaccine.
7. c. NSAIDs can cause irritation and damage to the gastrointestinal lining, resulting in gastrointestinal bleeding.
8. a. Red meat is high in purines, which can increase uric acid levels and exacerbate gout symptoms.
9. c. In active immunity, the body's immune system actively responds to the presence of an antigen, such as a vaccine, and produces its own antibodies. The client receives long-lasting protection from future infections due to the development of memory cells. On the other hand, passive immunity involves the transfer of pre-formed antibodies from an external source, such as immune globulin or maternal antibodies, providing immediate but temporary protection.
10. d. Divide the prescribed dose (40 mg) by the concentration of the adalimumab solution (40 mg/0.8 mL); $40 \text{ mg} \div 40 \text{ mg}/0.8 \text{ mL} = 0.8 \text{ mL}$.

Chapter 7

Case Study

1. a. This question is important to determine whether he has had a recent positive or negative result before today's visit.
2. c. Tuberculosis is a mycobacterium and will not grow on the other types of cultures listed.

Review Questions

1. a. Ceftriaxone is the treatment of choice for gonorrheal infections.
2. c. It is important that clients receive the HPV vaccine before becoming sexually active, if possible, to provide maximal protection against the HPV strains most likely to cause cancer.
3. b. A toxic effect of ethambutol is the loss of ability to distinguish between the colors red and green, warranting a change in drug therapy.
4. d. Multiple tuberculosis medications are hepatotoxic, so liver function is essential to monitor.
5. c. Lindane is the only listed agent that acts against lice infestation.
6. a. The CD4 count determines the degree of immune system degradation that has occurred, with lower values indicating worsened immune function. HIV viral load is not a laboratory test.
7. b. Elvitegravir is the only listed agent that works as an integrase inhibitor to prevent the incorporation of viral DNA into human DNA.
8. d. Sulfamethoxazole contains a sulfonamide group and could cause a cross-sensitivity in the client.
9. c. *Clostridioides difficile* is responsible for causing colitis and severe diarrhea after taking clindamycin.
10. d. Tetracyclines should not be used if the client is pregnant.

Chapter 8

Unfolding Case Study

1. c. Guadelupe is of childbearing age. It is important to confirm she is not pregnant prior to initiating chemotherapy, as these agents can have harmful effects on the fetus.
2. a. Adjuvant therapy is given after initial treatment with surgery or radiation.
3. b. Taxol and other taxenes are likely to cause hypersensitivity reactions in clients receiving them. Premedicating the client with certain medications such as steroids, diphenhydramine, and histamine blockers will decrease the risk of these reactions.
4. a. Tamoxifen is an antiestrogen hormonal agent. Taking this medication will result in amenorrhea, or the absence of menstrual cycles.

Review Questions

1. c. Targeted therapy is administered to selectively kill cancer cells without harming healthy cells.
2. a. The nurse should continue with the treatment because the client's lifetime total of doxorubicin is within the maximum lifetime limit of 550 mg/m^2.
3. a. Leucovorin is administered with fluorouracil to enhance the effectiveness of fluorouracil.
4. d. To avoid infection, the client with myelosuppression should avoid cat litter boxes.
5. c. Pembrolizumab heightens T-lymphocyte activity, predisposing clients to the development of immune-mediated conditions.
6. c. Tumor lysis syndrome occurs when cancer cells are destroyed, releasing cellular debris and electrolytes into the blood, resulting in hypocalcemia, hyperkalemia, hyperphosphatemia, and acidosis.
7. d. Tamoxifen, an antiestrogen administered to treat breast cancers that are hormone-receptor positive, is taken for 5 years.
8. b. Doxorubicin should not be administered to clients who have a left ventricular ejection fraction less than 55%. Since this client has an ejection fraction of 58%, the nurse would administer the medication as prescribed.
9. b. Because this client has a low absolute neutrophil count, the nurse anticipates an order for filgrastim to stimulate stem cell production of white blood cells.
10. a. Rituximab has a high risk for causing a sensitivity reaction, so the client must be premedicated with diphenhydramine and acetaminophen.

Chapter 9

Review Questions

1. b. The central nervous system (CNS) is composed of the brain and the spinal cord. Therefore, the nurse would recognize that an ischemic stroke involves deficits originating in the CNS.
2. d. The cerebellum, located below the cerebrum, controls coordination of movement and postural adjustment.
3. a. The cervical vertebrae are located in the neck region of the body.
4. d. The autonomic nervous system regulates involuntary responses by regulating cardiac muscle and smooth muscle contraction in addition to gland activity.
5. c. The parasympathetic nervous system, or "rest and digest" system, is activated when the body is relaxed and not under actual or perceived stress.
6. b. The sympathetic nervous system, or "fight or flight system," is activated when the body is under actual or perceived stress to ready the body's response to a potential threat.
7. b. Neurotransmission is the nervous system's communication process by which electrical signals are sent down the axon and transformed into chemical messengers.
8. a. The most common neurotransmitters of the autonomic nervous system are acetylcholine and norepinephrine.
9. b. Medications that stimulate the release of acetylcholine are known as parasympathomimetic due to their mimicking of the parasympathetic nervous system.
10. d. The beta1 adrenergic receptor would be indicated in this instance. Specifically, this medication would be a beta1 blocker.

Chapter 10

Case Study

1. c. These drugs prevent the enzyme cholinesterase from breaking down ACh, allowing more of this neurotransmitter to accumulate in the synapses and continuing to stimulate the cholinergic receptors at the NMJ. This stimulation causes increased skeletal muscle contraction.
2. b. MG is an autoimmune disease in which the client produces antibodies that destroy functional receptors at the NMJ, causing muscle weakness.

Review Questions

1. a. The drug will cross the blood–brain barrier, has a 70-hour half-life, and is unaffected by oral intake.
2. b. Because a decreased level of ACh is present in this disease, decreasing the action of AChE can help reduce the symptoms because less ACh will be broken down.
3. a. The patch needs to be changed every 24 hours, not weekly. All the other options are correct statements.
4. b. Memantine is an NMDA receptor antagonist. When too much calcium enters the cell, it makes it extremely excitable, interfering with cognition. Too much calcium is toxic. Normally, glutamate binds to the NMDA receptors for a brief period, allowing the calcium channel to open. Glutamate then dissociates from the receptors and magnesium binds to the NMDA receptors, closing the calcium channel and preventing further calcium from entering.
5. c. Propranolol is a nonselective beta blocker; therefore, one would be concerned about extremely low heart rate plus bronchoconstriction.
6. b. There is a potential for serious and life-threatening skin rashes when using this drug. Stevens–Johnson syndrome, a disorder of the skin and mucous membranes characterized by a painful rash that disseminates, is one example. Blisters form, and eventually the top skin layer will die and shed.
7. c. The drug was prescribed as a disintegrating tablet, so it must completely dissolve on the tongue. It is not to be chewed, crushed, or swallowed whole.
8. d. The AChE inhibitors prescribed for myasthenia gravis increase muscle strength and muscle relaxation. Since clients may have drooping of the eyes due to muscle weakness, the ability to raise the eyelids independently is evident of increased muscle strength.
9. c. Because the client's dose was increased, they are at risk for cholinergic crisis. This is characterized by increased urine output, diarrhea, vomiting, excess salivation, and diaphoresis.
10. b. If there is cholinergic toxicity, an anticholinergic should be given to counteract the signs and symptoms. For instance, atropine will increase the heart rate and decrease intestinal motility and inhibit contraction of the detrusor muscle.

Chapter 11

Case Study

1. c. This is concerning because this drug has the potential to exacerbate dysrhythmias.
2. a. This drug is a cholinergic blocker (anticholinergic). According to the Beers Criteria®, these drugs should not be used in those over the age of 60 years and with a history of BPH that causes urinary retention. This could worsen from the anticholinergic.

Review Questions

1. b. The nurse is evaluating the therapeutic effectiveness of the drugs. The client being able to perform more activities of daily living indicates the drugs are working.
2. b. Because the client cannot swallow well, this drug is the best to meet their needs. It is available in a patch form and is administered transdermally.
3. c. This client is experiencing neuroleptic malignant syndrome.
4. c. This drug can be used to manage relapses in clinically isolated syndrome (CIS), primary progressive (PPMS), relapsing-remitting (RRMS), and secondary progressive (SPMS).
5. a. Insomnia occurs with this drug because it metabolizes to methamphetamine and amphetamine, causing stimulation. If taken too late in the day, sleep could be disrupted.
6. c. This drug can exacerbate tuberculosis. If a tuberculin skin test and chest radiograph (x-ray) are positive, the client must be treated for TB before starting the prescribed drug.
7. b. High-protein meals will interfere with levodopa absorption and entrance into the brain.
8. d. This drug causes euphoria, which can diminish impulse control.
9. c. Benztropine is an anticholinergic. One of the adverse effects of this classification is the potential to increase intraocular pressure; therefore, it should be avoided in clients with glaucoma.
10. a. These block dopamine receptors in the striatum, resulting in diminished therapeutic effects of levodopa and augmented Parkinsonian symptoms.

Chapter 12

Review Questions

1. a. Mannitol is administered for cerebral edema and increased intracranial pressure. Elevating the head of the bed to a 30-degree angle and keeping the client's head in a neutral position helps to decrease intracranial pressure.
2. c. $\frac{300 \text{ mg}}{x \text{ mL}}$ desired dose $= \frac{250 \text{ mg}}{5 \text{ mL}}$ supply on hand
$$250x = 300(5)$$
$$x = \frac{1500}{250}$$
$$x = 6 \text{ mL per dose.}$$
3. b. Sumatriptan is contraindicated in pregnancy, and contraception should be taken while on this drug.
4. a. Valproic acid is a valproate, which is used in the treatment of seizures and as a mood stabilizer.
5. b. $\frac{70 \text{ mg}}{x \text{ mL}}$ desired dose $= \frac{50 \text{ mg}}{1 \text{ mL}}$ supply on hand
$$50x = 70(1)$$
$$x = \frac{70}{50}$$
$$x = 1.4 \text{ mL per dose.}$$
6. d. Rash is an adverse effect of ethosuximide.
7. b. Migraine headache symptoms can last for several hours up to several days.
8. d. The normal intracranial pressure for a client in a vertical position is 7–15 mm Hg.
9. a. Acetazolamide is an osmotic diuretic and is used in the treatment of cerebral edema, intracranial hypertension, and to lower increased intracranial pressure.
10. d. Levetiracetam is used in the treatment of seizures and causes adverse effects such as behavioral symptoms of hostility and aggression as well as psychotic symptoms of hallucinations and delirium.

Chapter 13

Case Study

1. b. Fluoxetine has a stimulant effect and may interfere with sleep if taken close to bedtime. Therapeutic effects take 4–6 weeks.
2. a. If someone has an undiagnosed bipolar disorder, placing them on an antidepressant without a mood stabilizer can induce mania.

Review Questions

1. b. The drug blocks muscarinic receptors and causes anticholinergic effects. This results in reduced salivation (xerostomia), decreased peristalsis (constipation), and relaxation of the detrusor muscle, causing urinary retention.
2. b. Rapid, pressured speech is a classic sign of mania. If the drug level is considered subtherapeutic, this means it is not working favorably. The other options indicate the manic behavior is being well managed.
3. c. This demonstrates the child's ability to remain focused on the task at hand.
4. c. The brain has to adapt to these types of drugs. Although a person can feel some benefit in 2 weeks, full effects can take 4–6 weeks. It is important to emphasize this to the client or else they will simply stop taking the drug.
5. b. Tremors, pseudoparkinsonism, and akinesia are extrapyramidal side effects that can occur with haloperidol.
6. d. Whole milk and aged cheeses are high in tyramine and therefore should be avoided.
7. c. Clozapine can cause a significant decrease in the neutrophil count, increasing the risk of infection. Also, abrupt discontinuation of clozapine can result in significant complications for client treatment. To ensure the client does not have a gap in the treatment, this is a modification to the REMS program.
8. c. This is a norepinephrine dopamine reuptake inhibitor. SSRIs, SNRIs, and MAOIs all cause some degree of sexual dysfunction.

9. a. Zolpidem is useful for initiating sleep (sleep latency) and ensuring the client stays asleep during the night.
10. a. Because this drug is a stimulant, it should not be taken near the evening or it will interrupt sleep.

Chapter 14

Unfolding Case Study

1. c. Because this client is taking both aspirin and ibuprofen (which are both NSAIDs), and because she is taking ibuprofen on an as-needed basis, it is important to determine how much ibuprofen the client is taking.
2. d. This dose exceeds the 3200 mg maximum dose for ibuprofen and, based on the client's report of black tarry stools, has already caused gastric bleeding.
3. c. Hydromorphone is a semisynthetic derivative of morphine that is used to treat moderate to severe pain.
4. a. The use of an opioid, such as hydromorphone, with alcohol can result in sedation and respiratory depression.

Review Questions

1. b. The client's pain is considered chronic because it has been going on for more than 3 months.
2. c. Pain is a subjective rating, and the nurse should define pain as "whatever the client says it is." Therefore, the nurse should administer the pain medication.
3. d. Eight tablets of 500 mg acetaminophen is 4000 mg, which is the amount of acetaminophen that should not be exceeded in a day.
4. c. Ibuprofen is the only option that is an anti-inflammatory drug.
5. b. The affected nerves were damaged by the varicella-zoster virus. Shingles pain, or postherpetic neuralgia, develops in up to 50% of individuals over the age of 65 who contract the disease.
6. b. Naloxone works as an opioid receptor antagonist and is the drug of choice to quickly reverse the effects of opioid intoxication, which is indicated here by the client's unresponsiveness and shallow breathing.
7. d. This client most likely experienced a reaction to histamine caused by morphine. This adverse reaction is most often seen with morphine and codeine, which is converted into morphine.
8. b. Naltrexone is an opioid antagonist that can be used orally and intramuscularly to aid clients who are attempting to quit using opioids. While the client is taking naltrexone, any opioids taken will not be able to activate opioid receptors, blunting the effects of opioids and the feelings of euphoria.
9. b. Tolerance is a natural occurrence in clients receiving chronic opioid agonists. It frequently requires the dosage of the opioid agonist to be increased to achieve adequate pain management.
10. c. Severe shivering with chills (also known as rigors) may occur in clients who received anesthesia. The treatment of choice for this is meperidine. Because of the well-known toxicities of meperidine in older adults and those with poor renal function, it should almost never be used for pain.

Chapter 15

Unfolding Case Study

1. b. This is important to assess in case the client is prescribed buprenorphine or naltrexone to avoid withdrawal symptoms.
2. d. Diarrhea is a common symptom of opioid withdrawal and can occur if clients continue to use opioids while taking the opioid antagonist naltrexone.
3. a. This is the only medication of the four listed that is indicated for smoking cessation.
4. b. The client's quit date should be one week after starting varenicline, to reduce withdrawal symptoms and increase chances for successful cessation.

Review Questions

1. c. This client had a sudden discontinuation of their oxycodone, leading to typical opioid withdrawal effects.
2. d. This client is experiencing the behavioral aspects of discontinuation of a substance, leading to intense cravings.
3. b. The Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) uses a symptoms-based approach to manage the symptoms of alcohol withdrawal as they occur.

4. a. This client is experiencing the triad of opioid overdose symptoms (respiratory depression, CNS depression, and miosis). This client requires quick reversal of these effects, so naloxone should be administered.
5. c. The naloxone in this drug makes it so that if it is injected instead of being used orally, it will prevent the buprenorphine from causing as much euphoria as it would by itself.
6. a. Because of the short-acting nature of naloxone, it is imperative to call emergency services after naloxone administration to get definitive care prior to the client re-sedating.
7. b. Facial flushing is one of the most characteristic reactions seen in clients consuming alcohol while using disulfiram.
8. d. Seizures are one of the most severe and potentially life-threatening effects that can be seen with alcohol withdrawal.
9. c. This is an important counseling point to avoid having the client receive excessive doses of nicotine, leading to toxicity.
10. a. Because bupropion is primarily used as an antidepressant and can reduce cravings during smoking cessation, it is an ideal medication to treat both conditions.

Chapter 16

Review Questions

1. c. The QRS complex represents ventricular depolarization, which occurs as the electrical impulse moves through the ventricle to prompt contraction.
2. a. The right ventricle pumps blood into the pulmonary artery and is subject to increased pressure in clients with pulmonary arterial hypertension.
3. b. The coronary arteries supply the heart tissue with blood.
4. d. With the exception of the pulmonary artery, all arteries carry oxygenated blood to various tissues for use.
5. b. Both ventricles pump nearly simultaneously (ventricular systole). While the ventricles are pumping, both of the atria are filling (atrial diastole). The atria do not pump simultaneously with the ventricles.
6. a. The signal starts in the sinoatrial node and passes through the atrioventricular node to get to the ventricles. From there, it travels through the bundles of His and Purkinje fibers.
7. c. Automaticity is when the tissue is able to spontaneously generate an action potential, leading to spontaneous depolarization. Tissues with automaticity can act as the pacemaker of the heart.
8. a. The ECG gives information about heart rhythm; abnormal rhythms are known as arrhythmias or dysrhythmias. Although some information about structural heart disease can be garnered from an ECG, other diagnostic methods such as echocardiography or biopsy would be needed to confirm the remaining diagnoses.
9. d. The SA node, known as the pacemaker of the heart, has the property of automaticity and sends out electrical impulses 60–100 times/minute.
10. d. Bradycardia describes a slow heart rate (less than 60 beats per minute), and tachycardia describes a fast heart rate (faster than 100 beats per minute).

Chapter 17

Case Study

1. c. Based on the ECG data (no discernable P waves and narrow QRS complexes) and heart rate (greater than 100 beats per minute), the client has atrial fibrillation with rapid ventricular response.
2. d. Beta-adrenergic blockers such as metoprolol are an option for treating atrial fibrillation with rapid ventricular response.

Review Questions

1. c. Metoprolol is a beta-adrenergic blocker that slows the heart rate. If a client takes too much metoprolol, they may experience bradycardia.
2. c. Verapamil is a nondihydropyridine calcium channel blocker. It can decrease cardiac contractility, which can exacerbate congestive heart failure.
3. b. Procainamide is a sodium channel blocker antidysrhythmic drug, but it also has activity as a potassium

channel blocker. Potassium blocker drugs require monitoring of the QT interval.

4. d. Quinidine is associated with a high incidence of diarrhea. Because diarrhea can cause electrolyte abnormalities, excessive diarrhea should be reported to the health care provider.
5. b. Metoprolol is a beta-adrenergic blocker. Beta-adrenergic blockers can cause fatigue.
6. a. Potassium channel blockers slow repolarization and are associated with torsade de pointes, a serious ventricular dysrhythmia.
7. b. Amiodarone can cause photosensitivity resulting in a bluish-gray color of sun-exposed skin.
8. b. Metoprolol tartrate does not require inpatient initiation. Dofetilide and sotalol require inpatient initiation. Mexiletine is used for ventricular arrhythmias.
9. c. Diltiazem and verapamil have FDA warnings concerning interactions with simvastatin. Diltiazem and verapamil inhibit the metabolism of simvastatin, increasing simvastatin plasma levels and the risk for adverse effects.
10. a. Because digoxin is eliminated by the kidneys, acute kidney injury puts the client at risk for digoxin toxicity. Some symptoms of digoxin toxicity are stomach upset, visual changes, and confusion.

Chapter 18

Unfolding Case Study

1. c. Based on the American Heart Association Blood Pressure Category criteria, the client has hypertension stage 2 (systolic blood pressure 140 mm Hg or higher and diastolic blood pressure 90 mm Hg or higher).
2. c. Renal function tests are likely to be ordered for Hahn to evaluate the function of her kidneys because both hypertension and diabetes can cause kidney damage. Kidney function should also be evaluated before starting pharmacological treatment for hypertension.
3. c. ACE inhibitors, such as enalapril, can cause hyperkalemia (an elevated serum potassium level), so the nurse should advise the client not to use potassium-containing salt substitutes.
4. b. The client who smokes should be advised to stop smoking to aid in blood pressure control and reduce the risk for coronary artery disease. Other nonpharmacologic treatments for hypertension include weight reduction, salt restriction, exercising 30–40 minutes four times/week, and limiting alcohol intake.
5. d. Constipation is an adverse effect of verapamil, so the nurse instructs Hahn to increase her daily fiber intake to help reduce this effect.
6. a. In a heart-healthy diet, the client should reduce her intake of red meat. This statement indicates a need for further teaching.

Review Questions

1. d. Hypertension stage 2 is classified as a systolic blood pressure of 140 mm Hg or higher or a diastolic blood pressure of 90 mm Hg or higher.
2. b. Benazepril is an ACE inhibitor and may be used alone or in combination with other drugs in the management of hypertension and heart failure. A therapeutic effect of the medication is a normal blood pressure reading; 126/76 mm Hg falls within the AHA guidelines for normal blood pressure.
3. a. Nadolol is a nonselective beta-adrenergic blocker used to treat hypertension and other cardiac disease processes. Nadolol inhibits beta 1 and beta 2. Blockade of beta 2 receptors in the lungs causes bronchospasm; thus, nadolol is contraindicated in clients with asthma.
4. b. $0.1\text{ g} = 100\text{ mg}$. $100\text{ mg} \div 50\text{ mg} = 2$ tablets.
5. d. Transdermal nitroglycerin is prescribed as a maintenance medication for stable angina, which takes 30–60 minutes for therapeutic effects to begin. The patch should be applied around the same time every day and worn for 12–14 hours and then removed for 10–12 hours to avoid client tolerance.
6. d. Verapamil is a calcium channel blocker. Grapefruit juice increases blood levels of verapamil by inhibiting its metabolism. The excess amount of medication can intensify the medication's hypotensive effect, placing the client at an increased risk for syncopal episodes.
7. b. Hydrochlorothiazide is a thiazide diuretic and can deplete potassium levels in the body. Clients should eat foods rich in potassium. Clients should monitor themselves for signs of hypokalemia such as fatigue, tachycardia, muscle weakness, and leg cramps.
8. b. $6.25\text{ mg} \div 3.125\text{ mg} = 2$ tablets per dose.

9. d. Losartan is a selective and competitive angiotensin II receptor blocker (ARB) at the angiotensin I receptor.
10. a. Carvedilol is a beta-adrenergic blocker and slows the heart rate. A side effect of carvedilol is bradycardia. The health care provider should be notified of bradycardia in a client before the administration of the drug.

Chapter 19

Case Study

1. c. Enalapril is an ACE inhibitor that can cause hyperkalemia (a high potassium level).
2. b. Furosemide is a loop diuretic and is used to decrease fluid volume.

Review Questions

1. d. Cardiac output is composed of heart rate × stroke volume. Normal resting cardiac output is 4–5 liters per minute.
2. d. Lisinopril inhibits the enzyme that converts angiotensin I to angiotensin II.
3. c. $7.5 \text{ mg} \div 2.5 \text{ mg} = 3 \text{ tablets}$.
4. c. Sacubitril inhibits neprilysin, which is an enzyme that breaks down BNP. BNP stimulates vasodilation and sodium and water excretion, which decrease afterload and preload, respectively.
5. a. Valsartan and spironolactone can cause potassium to be reabsorbed in the nephron. Clients are at risk for hyperkalemia.
6. c. Dapagliflozin is a sodium-glucose cotransporter 2 inhibitor and has received FDA approval for use in the treatment of heart failure.
7. c. $60 \text{ mg} \div 40 \text{ mg} = 1.5 \text{ or } 1\frac{1}{2} \text{ tablets}$.
8. c. Research has shown that beta blockers and medications affecting the RAAS do not work as well in the treatment of heart failure for Black clients as hydralazine and isosorbide dinitrate do.
9. d. Digoxin is a cardiac glycoside and slows the heart rate. It can cause bradycardia. The health care provider should be notified before administering this drug.
10. b. Ivabradine is an I(f) current inhibitor. Grapefruit juice increases blood levels of ivabradine by inhibiting its metabolism. The excess amount of medication can intensify the medication's hypotensive effect, placing the client at an increased risk for syncopal episodes.

Chapter 20

Case Study

1. c. The PTT is 75 seconds. Per the protocol, any PTT between 71 and 90 seconds will require a decrease in the heparin rate by 2 units/kg/hour.
2. b. One of the advantages of LMWH is the longer duration of action, which means that once-daily injections, instead of continuous infusion, are effective.

Review Questions

1. a. Heparin can be monitored by using the partial thromboplastin time or anti-factor Xa level, depending on the institutional protocol.
2. a. Protamine is a protein that works to neutralize heparin.
3. c. The antibodies decrease the platelet count, leaving the client at risk for the development of thrombosis.
4. b. Alteplase is a thrombolytic drug used to dissolve clots.
5. d. Heparin is an anticoagulant. It will prevent further clot formation while the body naturally breaks down the clot, but it will not directly dissolve the clot.
6. d. Clients taking warfarin must maintain a consistent amount of vitamin K in their diet.
7. b. Warfarin is monitored using the INR, or international normalized ratio.
8. b. Heparin-induced thrombocytopenia is characterized by a decreased platelet count. Contrary to typical thrombocytopenia, the client is extremely hypercoagulable and often has a thrombosis such as a deep vein thrombosis.
9. c. This drug is more effectively absorbed when taken with food.
10. b. Severe uncontrolled hypertension is a contraindication to alteplase administration.

Chapter 21

Review Questions

1. b. Medications can be used to decrease cholesterol levels but are not intended to increase triglyceride levels.
2. b. Alirocumab is a monoclonal antibody that is self-administered by the client.
3. d. Fenofibrate is indicated to treat hypertriglyceridemia. Fibrates stimulate lipoprotein lipase to break down triglycerides.
4. c. Flushing can be mitigated by taking an NSAID 30 minutes before taking niacin or by switching to an extended-release product.
5. b. The therapeutic effect of ezetimibe is that of lowering LDL-cholesterol via decreased cholesterol absorption.
6. c. Cholestyramine is a bile acid sequestrant available as a powder. It must be mixed with fluid prior to administration.
7. c. Rosuvastatin at a dose of 20–40 mg daily is considered a high-intensity statin medication.
8. a. Pravastatin is considered a hydrophilic statin. It can less easily enter the muscle, which may confer a lower risk of myalgia.
9. d. Ezetimibe is an appropriate combination therapy with statin medications. Gemfibrozil is contraindicated for use with rosuvastatin. Rosuvastatin does not need to be taken at bedtime because it has a long half-life.
10. a. This drug may cause severe myopathy, which can lead to rhabdomyolysis.

Chapter 22

Case Study

1. a. Nitroglycerin dilates coronary arteries, which increases oxygen delivery to the heart tissue, thereby reducing chest pain.
2. c. A history of asthma is a contraindication to taking aspirin.

Review Questions

1. b. Morphine is a potent opioid agonist and can cause respiratory depression and failure. It is very important to monitor the client frequently (reassess at least every 5–10 minutes) when using morphine to control chest pain.
2. c. Nitroglycerin is a vasodilator, and vasodilation causes the blood pressure to drop.
3. a. Adenosine has a very short half-life and should be administered as a rapid IV bolus directly into a vein over 1–2 seconds, followed by a rapid saline flush.
4. c. The nurse should ask whether the client is taking any medications for erectile dysfunction because the use of nitroglycerin is contraindicated in clients who are taking a phosphodiesterase inhibitor such as tadalafil or sildenafil.
5. a. Stable angina occurs during exercise or exertion and improves with rest. Stable angina presents when the heart needs more oxygen but the supply of oxygen is restricted. Once the heart does not need increased oxygen, the angina subsides.
6. b. The ordered dose of diltiazem is 0.25 mg/kg, and $176 \text{ lb} \div 2.2 \text{ kg} = 80 \text{ kg}$, so $0.25 \text{ mg/kg} \times 80 \text{ kg} = 20 \text{ mg}$.
7. a. The therapeutic effects of epinephrine include bronchodilation, increased heart rate, and increased blood pressure.
8. b. Dopamine causes vasospasm and can lead to necrosis, sloughing, and potentially gangrene if extravasation into the tissue occurs at the IV site.
9. d. Prolonged use of procainamide may lead to a positive antinuclear antibody test; if this occurs, the risk–benefit ratio of procainamide use should be reassessed.
10. a. Epinephrine is administered intramuscularly for the client in anaphylaxis who does not have ventricular fibrillation, pulseless ventricular tachycardia, asystole, or pulseless electrical activity.

Chapter 23

Review Questions

1. b. The symptoms presented are classic signs of rhinitis.
2. a. Asthma is characterized as difficulty moving air into and out of the lungs due to bronchoconstriction. This causes wheezing during inspiration and expiration.
3. d. Chronic bronchitis is characterized by chronic cough and sputum production. The most common cause is smoking.
4. a. Identifying triggers will help the client decrease symptoms by avoiding the trigger items.
5. d. Emphysema develops gradually, and many clients have no symptoms at first. Most clients notice shortness of breath when doing normal activities.
6. a. Clients with COPD are more prone to respiratory infections, so they should implement infection prevention strategies.
7. b. Oxygen saturation is the amount of oxygen bound to hemoglobin.
8. a. Emphysema and COPD are most often caused by cigarette smoking.
9. b. Quitting smoking will not cure the disease, but it can prevent more damage.
10. c. Sinus pain and pressure are common symptoms of sinusitis. Using pain reducers such as acetaminophen or ibuprofen can help with these symptoms.

Chapter 24

Review Questions

1. b. This is a second-generation antihistamine that does not cause drowsiness. Clients who are driving or operating machinery can safely take this medication.
2. a. Guaifenesin is indicated for nonproductive coughs. The nurse should reassess the client to determine if the cough is productive and an alternative medication should be considered.
3. c. Acetylcysteine is also indicated for clients suffering from acetaminophen toxicity.
4. c. Oxymetazoline should not be used for more than 3 days because of the chance of rebound congestion.
5. d. Opioid antitussives inhibit coughing by exerting their effects on the central nervous system. This increases the client's risk of respiratory depression.
6. a. Grapefruit juice should be avoided when taking dextromethorphan because it can increase its action.
7. c. Constricting blood vessels in the nose decreases the amount of fluid draining from the blood vessels into the nasal passage.
8. c. It works by blocking histamine responses at H1 receptors.
9. c. $\frac{50 \text{ mg}}{x \text{ mL}}$ (desired dose) $= \frac{25 \text{ mg}}{1 \text{ mL}}$ (supply on hand)
$$25x = 50 \times 1$$
$$x = \frac{50}{25}$$
$$x = 2 \text{ mL per dose.}$$
10. b. $\frac{10 \text{ mg}}{x \text{ tablets}}$ (desired dose) $= \frac{5 \text{ mg}}{1 \text{ tablet}}$ (supply on hand)
$$5x = 10 \times 1$$
$$x = \frac{10}{5}$$
$$x = 2 \text{ tablets per dose.}$$

Chapter 25

Unfolding Case Study

1. b. Based on Harold's smoking history, decreased breath sounds, prolonged expiration, and mild wheezing, the nurse should anticipate a diagnosis of COPD.
2. a. Beta-adrenergic agonists, such as salmeterol, are often used as part of long-term management for COPD. They provide bronchodilation and help improve airflow by relaxing the airway smooth muscles.

3. a. Corticosteroids like beclomethasone work to reduce and prevent inflammation in the airways.
4. d. Corticosteroids can cause the adverse reaction of candidiasis. Rinsing the mouth helps to prevent candidiasis.

Review Questions

1. c. Albuterol is a short-acting beta-agonist that works by stimulating beta-2 adrenergic receptors in the airway smooth muscles.
2. a. $60 \div 3 = 20.$
3. c. Theophylline is a xanthine derivative medication used for long-term control of asthma symptoms.
4. c. Ipratropium bromide is a respiratory anticholinergic medication that acts by blocking the action of acetylcholine, a neurotransmitter that causes bronchoconstriction. By blocking acetylcholine, ipratropium bromide helps to relax the smooth muscles in the airways, leading to bronchodilation and improved airflow.
5. d. First the nurse needs to determine the client's weight in kilograms:
$121 \text{ lb} \div 2.2 \text{ kg} = 55 \text{ kg}. \ 55 \text{ kg} \times 4.6 \text{ mg/kg} = 253 \text{ mg}.$
6. c. The most commonly reported side effects of montelukast include headache and dizziness.
7. d. Respiratory anticholinergic medications have the potential to worsen urinary retention due to their ability to relax smooth muscles, including those in the urinary tract.
8. c. Abruptly stopping methylprednisolone, a corticosteroid medication, can lead to adrenal insufficiency. Long-term use of corticosteroids suppresses the adrenal glands, causing them to produce less cortisol. When the medication is abruptly discontinued, the adrenal glands may not be able to produce enough cortisol on their own, leading to adrenal insufficiency.
9. a. Salmeterol is a long-acting beta-agonist that is not intended for quick relief during an asthma attack.
10. c. Tiotropium is an anticholinergic medication that works by blocking the action of acetylcholine, a neurotransmitter that causes bronchoconstriction. By blocking acetylcholine, tiotropium helps to relax the smooth muscles in the airways, leading to bronchodilation and improved airflow.

Chapter 26

Review Questions

1. a. A decrease in vasopressin production leads to normal glucose levels, an increased loss of water in the urine resulting in polyuria, an increased thirst (polydipsia), and an increased hunger (polyphagia).
2. b. CRH stimulates the release of adrenocorticotropic hormone from the anterior pituitary gland, which stimulates the release of cortisol from the adrenal cortex, decreasing cortisol production and leading to a decrease in the body's stress response.
3. a. $\frac{150 \text{ mcg}}{3 \text{ doses}} = \frac{50 \text{ mcg}}{1 \text{ dose}}$
$\frac{50 \text{ mcg}}{x \text{ mL}}$ (desired dose) $= \frac{100 \text{ mcg}}{1 \text{ mL}}$ (supply on hand)
$100x = 50 \times 1$
$x = \frac{50}{100}$
$x = 0.5 \text{ mL per dose.}$
4. b. Hydrocortisone is a steroid drug that can cause hyperglycemia and increase blood pressure. Monitoring for these potential adverse effects is essential to ensure client safety.
5. d. Acromegaly is a disorder caused by excessive growth hormone secretion from the pituitary, which results in abnormal growth of bones and soft tissues.
6. a. Fludrocortisone is a mineralocorticoid that can cause hypokalemia and hypertension. Monitoring for these adverse effects is essential to ensure client safety.
7. a. $\frac{120 \text{ mg}}{x \text{ mL}}$ (desired dose) $= \frac{125 \text{ mg}}{2 \text{ mL}}$ (supply on hand)
$125x = 120 \times 2$
$x = \frac{240}{125}$
$x = 1.92 \text{ mL};$
therefore, the nurse should administer 1.9 mL per dose.

8. b. Glucocorticoid medications require a tapering dose to allow the adrenal glands to resume their normal function.
9. d. Bromocriptine is contraindicated in clients with uncontrolled hypertension.
10. b. In hyperaldosteronism, the kidneys reabsorb too much sodium and excrete too much potassium, leading to an increased blood volume and blood pressure and decreased potassium levels.

Chapter 27

Case Study

1. b. This client with hyperthyroidism is showing evidence of toxicity to methimazole. Manifestations of methimazole toxicity are similar to those of hypothyroidism and include cold intolerance, weight gain, fatigue, lack of energy, bradycardia, and depression.
2. d. TSH, T3, and T4 laboratory tests are used to determine hypothyroidism.

Review Questions

1. c. Symptoms of hyperthyroidism include weight loss, heat intolerance, diarrhea, fine tremor, tachycardia, frequent mood changes, and muscle weakness.
2. d. Clients with hypothyroidism will have an elevated TSH level.
3. d. Methimazole is an antithyroid drug used to treat hyperthyroidism.
4. c. Soy has a food interaction with levothyroxine and can decrease its effectiveness.
5. c. An increase in energy is a therapeutic effect of levothyroxine.
6. c. The phosphate level is above the expected reference range. Phosphate levels are increased in clients with hypoparathyroidism.
7. a. Bone pain, along with muscle weakness and depression, are signs of hyperparathyroidism.
8. a. Alendronate may cause esophagitis, which can lead to dyspepsia.
9. b. First, convert 0.275 mg to mcg, $0.275 \text{ mg} \times 1000 \text{ mcg/mg} = 275 \text{ mcg}$

$$\frac{275 \text{ mcg}}{x \text{ tablets}} \text{ (desired dose)} = \frac{137 \text{ mcg}}{1 \text{ tablet}} \text{ (supply on hand)}$$

$$137x = 275 \times 1$$

$$x = \frac{275}{137}$$

$$x = 2 \text{ tablets.}$$

10. b. 15 mg divided by three divided doses equals 5 mg each dose.

Chapter 28

Unfolding Case Study

1. c. Due to the client's age, gradual onset of symptoms and sedentary lifestyle, she will most likely be diagnosed with type 2 diabetes mellitus. This client's symptoms of fatigue, polyuria, thirst, and blurred vision are consistent with this diagnosis.
2. d. Glycosylated hemoglobin measures the average blood glucose level of an individual for the past 90 days. A reading of 6.5% or higher indicates diabetes.
3. a. Extended-release glipizide should be taken with the first meal of the day, not with dinner.
4. a. The client's glycosylated hemoglobin has dropped from 7.8% to 6.9%, below the goal of less than 7% for a person with diabetes. She has also lost 15 pounds in 6 months. The health care provider would not recommend changes in the treatment plan at this time.

Review Questions

1. d. A glycosylated hemoglobin greater than 6.5% represents diabetes.
2. b. Clients with diabetes should be taught to recognize signs of hypoglycemia to prevent a hypoglycemic reaction and serious complications.
3. a. The onset of regular insulin is 30 minutes. Breakfast should be given by 7 a.m. to prevent hypoglycemia.
4. b. Insulin glargine is a long-acting insulin.

5. c. Insulin isophane NPH peaks in 4–12 hours. The client is at risk for hypoglycemia during this time and should eat a snack to prevent hypoglycemia.
6. d. Glucagon is used to treat severe hypoglycemia when the client is semiconscious, unconscious, or unable to consume carbohydrates/sugar.
7. c. The nurse should combine the regular insulin and the NPH in the same syringe so a total of 38 units should be prepared, with regular insulin being drawn up first.
8. c. Only rapid-acting insulins should be administered via an insulin pump. Insulin aspart is a rapid-acting insulin.
9. a. Metformin should be held 24 hours prior to and 48 hours after contrast dye administration in clients with renal impairment.
10. a. $\frac{750 \text{ mg}}{x \text{ tablets}}$ (desired dose) $= \frac{500 \text{ mg}}{1 \text{ tablet}}$ (supply on hand)

$$500x = 750 \times 1$$
$$x = \frac{750}{500}$$
$$x = 1.5 \text{ tablets per dose.}$$

Chapter 29

Review Questions

1. a. Bile, secreted by the liver, aids in digestion by breaking down fats into fatty acids; therefore, the client may need to limit intake of dietary fat.
2. b. Gastritis, the irritation and inflammation of the lining of the stomach, can result in bleeding.
3. b. Saliva helps moisten food to make it easier to swallow. The salivary glands produce about 2 L of saliva every day to help keep the oral cavity, including the buccal membranes, moist.
4. c. A dysfunctional upper esophageal sphincter may allow food or fluid to enter the airway when the client swallows.
5. a. Because the small intestine is responsible for absorbing nutrients, the client will need vitamin and mineral supplements.
6. c. Lipase is involved in the breakdown of fats and the absorption of fat-soluble vitamins. This means the client will have deficient levels of vitamin K, a fat-soluble vitamin.
7. d. Intestinal villi are highly vascular and line the entire small intestine to accomplish most of the digestion and absorption processes. Therefore, dysfunctional villi may lead to malabsorption and nutritional deficiencies.
8. b. When assessing a client's gastrointestinal system, the nurse should ask whether the client has had any unintended weight gain or loss. A change in weight may be due to factors affecting the appetite or the ingestion, digestion, or absorption of nutrients.
9. c. Cranial nerve VII, the facial nerve, is involved with salivation.
10. a. When prostaglandin E_2 is not sufficient to prevent gastritis, medications such as antacids may be needed to reduce or eliminate symptoms.

Chapter 30

Case Study

1. c. Mineral oil is a lubricant laxative for constipation and fecal impaction.
2. a. Psyllium is a bulk-producing laxative that promotes natural elimination through water absorption and fiber that softens feces.

Review Questions

1. c. Dry mouth and other anticholinergic effects are common adverse effects of diphenoxylate with atropine.
2. b. The proper client positioning for suppository administration is lying on their left side with their right knee raised to their chest.
3. a. Chlorpromazine causes anticholinergic effects such as dry mouth, blurred vision, urinary retention and constipation.
4. a. Magnesium citrate is contraindicated with renal impairment due to a risk of hypermagnesemia.

5. d. Headache is a common side effect of ondansetron.
6. b. This medication should be taken with a full glass of water to promote effectiveness.
7. d. Clients with diarrhea should be assessed for signs and symptoms of dehydration, including decreased blood pressure and increased heart rate.
8. a. Linaclotide is contraindicated with a GI obstruction; it is used for constipation disorders.
9. c. Meclizine is an antiemetic and antivertigo agent that reduces the vestibular stimulation.
10. a. Scopolamine patches are used for motion sickness and should be applied 4 hours prior to traveling.

Chapter 31

Case Study

1. d. Famotidine is a medication used to treat peptic ulcer disease.
2. b. Famotidine is a histamine blocker that suppresses gastric acid by lowering the concentration of hydrogen ions. Alcohol, spicy foods, and NSAIDs increase gastric acid. Abruptly stopping a histamine blocker may cause rebound hyperacidity. Antacids should be taken 1–2 hours before or after other medications to avoid interfering with absorption. Histamine blockers often cause fatigue, not energy.

Review Questions

1. a. Aluminum hydroxide interferes with the absorption of many medications if taken at the same time.
2. d. Hypotension and cardiac arrhythmias are associated with the IV (parenteral) administration of cimetidine.
3. b. Omeprazole decreases pepsin, bile, and gastric acids.
4. a. Misoprostol can cause spontaneous abortion, premature birth, or birth defects.
5. b. Calcium carbonate may cause constipation and flatulence.
6. d. Calcium carbonate should be taken as needed when symptoms occur, after meals and before bedtime; it does not need to be taken every day.
7. a. Lansoprazole begins to reduce acid after approximately 2 hours, with ulcer symptom relief after about a week of use. The medication should be taken on an empty stomach and is typically used short-term (less than 6 months) for an ulcer.
8. a. Sucralfate adheres to the stomach lining for about 6 hours and will need to be repeated to ensure protection of the mucosal lining.
9. d. Antacids containing magnesium, such as magnesium hydroxide, can cause elevated magnesium levels.
10. c. The medication cannot be chewed and capsules cannot be opened, as the gastric acids will destroy the medication before it reaches the duodenum, where it is most effective.

Chapter 32

Case Study

1. b. Metabolic syndrome is a collection of risk factors such as hyperglycemia, hyperlipidemia, hypertension, and overweight/obesity.
2. d. Class III obesity is 40+ kg/m^2.

Review Questions

1. d. Overweight and obesity are determined by BMI. The BMI is calculated using height and weight.
2. b. BMI is calculated by dividing the client's weight by their height in inches squared and multiplying by 703: $278 \div 69^2 = 278 \div 4761 = 0.0584 \times 703 = 41.05$, rounded to 41.1.
3. b. Obesity and overweight are not the same; the distinguishing factor is a person's client's BMI. Overweight, with a BMI of 25–29, may lead to obesity. Obesity has a higher BMI ($\geq$30) and is associated with serious consequences.
4. a. Benzphetamine should not be given to clients who are pregnant; clients of childbearing age should be counseled to practice strict birth control methods to avoid pregnancy while on the medication.
5. d. Concurrent use of phenelzine, an MAOI, is contraindicated with phentermine. MAOIs should not be used 14 days before or after phenelzine use.
6. c. The dosage of phentermine/topiramate is usually readjusted every 14 days based on effectiveness.

7. a. The drug orlistat is available by prescription under the brand name Xenical or OTC under the brand name Alli.
8. c. Orlistat is not systemically absorbed and does not affect the cardiovascular and neurological systems. Common side effects are specific to the GI system—abdominal discomfort, flatus, nausea, oily rectal discharge, fecal urgency, fatty stool, and diarrhea.
9. d. Bupropion is an antidepressant, and naltrexone is an opioid antagonist; when combined, they have been effective in weight management.
10. c. Orlistat works by inhibiting the action of pancreatic lipase, an enzyme responsible for breaking down dietary fat in the small intestine. By blocking fat absorption, it reduces the number of calories absorbed from dietary fat, thus promoting weight loss.

Chapter 33

Review Questions

1. c. The creatinine level is viewed as a reasonable assessment of the GFR. Measurement of the actual GFR requires either an insulin infusion or radioisotope exposure.
2. d. The hydrostatic pressure in the glomerular capillaries promotes glomerular filtration, whereas the hydrostatic pressure in the Bowman's capsule and the oncotic pressure of the glomerular capillaries oppose glomerular filtration.
3. a. Risk factors for this type of incontinence include age, infection, and obstruction of the bladder outlet by an enlarged prostate gland.
4. d. The juxtaglomerular cells regulate the release of renin.
5. b. The parasympathetic stimulation contracts the detrusor muscle fibers in the bladder.
6. c. Increasing fluid intake decreases urine concentration, which in turn decreases the concentration of minerals in the urine that contribute to stone formation.
7. a. Fluid volume excess may be manifested by distention of the neck veins resulting from right heart failure.
8. c. Juxtamedullary nephrons comprise about 15% of all nephrons and are responsible for concentrating urine.
9. b. Functional incontinence occurs when an obstruction—such as a urethral obstruction due to enlargement of the prostate gland—interferes with bladder emptying and increases the post-void residual amounts.
10. a. Renal colic is the term most commonly used to describe the pain associated with kidney stones.

Chapter 34

Unfolding Case Study

1. c. The client is presenting with signs and symptoms of edema—weight gain and peripheral edema.
2. d. A chemistry panel measures key electrolytes and renal function tests.
3. b. Anuria is a contraindication to diuretic administration. Accordingly, decreasing urine output should be reported to the health care provider because it could indicate that the client's renal function is deteriorating.
4. b. Nonpharmacologic treatment for edema includes a low-sodium diet, walking, and elevating extremities to reduce swelling.
5. a. Green, leafy vegetables are an important part of a low-sodium diet with potassium-rich foods. This statement indicates a need for further teaching.
6. c. Thiazide diuretics can cause hypokalemia, which can cause changes in heart rate and rhythm.

Review Questions

1. c. The diuretic effect of furosemide can cause electrolyte abnormalities such as hyponatremia and hypokalemia, which cause weakness.
2. d. Amiloride is a potassium-sparing diuretic, so salt substitutes containing potassium should be avoided.
3. c. An eGFR value less than 60 mL/minute/1.73 m^2 for 3 months indicates chronic renal disease.
4. b. Mannitol is an osmotic diuretic that creates an osmotic gradient that pulls water from cells into the intravascular space.
5. b. Thiazide diuretics such as hydrochlorothiazide maintain serum calcium levels.
6. a. Mannitol is contraindicated for clients with heart failure. Lung congestion and peripheral edema are signs of

this condition for which the nurse needs to monitor.

7. d. Clients taking spironolactone are at risk for developing bradycardia.
8. a. The nurse should instruct the client to take diuretics in the morning to help prevent nocturia.
9. d. Loop diuretics cause potassium to be excreted and can be used for clients with hyperkalemia.
10. b. Diuretics such as furosemide have a threshold dose that is required for response, as well as a ceiling dose beyond which the diuretic effect will not increase.

Chapter 35

Review Questions

1. a. A potential adverse effect of trimethoprim and sulfamethoxazole is photosensitivity (increased sensitivity to sunlight or artificial light).
2. b. $200 \text{ mg} \div 100 \text{ mg tablets} = 2 \text{ tablets}$
3. c. Tadalafil works by relaxing the smooth muscles in the prostate and bladder, which can help improve urine flow and reduce the urinary symptoms caused by prostate enlargement.
4. c. Oxybutynin is an anticholinergic, and a common adverse effect is dry mouth (xerostomia) due to the inhibition of salivary gland secretions.
5. b. Phenazopyridine hydrochloride is a urinary analgesic that provides relief from the pain, burning, and discomfort associated with UTIs.
6. d. The vasomotor response of systemic vasodilation can occur if the client changes position rapidly, resulting in vertigo and syncope.
7. c. The pharmacologic action of mirabegron involves the selective activation of beta-3 adrenergic receptors in the bladder, leading to relaxation of the detrusor smooth muscle. This relaxation increases bladder capacity and decreases the urgency and frequency of urination.
8. a. Trimethoprim induces a progressive but reversible increase of serum potassium concentrations in a substantial number of clients.
9. d. Phenazopyridine hydrochloride is intended for short-term use to alleviate urinary pain and discomfort and should not be used longer than 2 days.
10. c. Solifenacin succinate is contraindicated in clients with narrow angle glaucoma.

Chapter 36

Case Study

1. c. Smoking is the most important because an estrogen-containing contraceptive can increase the likelihood of developing thrombophlebitis or thromboembolism.
2. d. The copper IUD is the longest-lasting contraceptive device and does not contain hormones. Because Susan is slightly overweight, has a smoking history, and has migraine headaches, any hormonal contraceptive may cause serious side effects.

Review Questions

1. a. Migraine headaches are a concern with contraceptive medications that contain progestins because they may exacerbate the headaches.
2. b. Oxytocin's effect on the kidneys can cause water intoxication and dilutional hyponatremia, which are considered significant side effects. Signs and symptoms of hyponatremia are related to the central nervous system (CNS) and musculoskeletal system.
3. d. Nitroglycerin is contraindicated when a client is using drugs for ED. The combination can cause significant hypotension and possible cardiac arrest.
4. a. Prepubescent clients on testosterone therapy may develop early closure of epiphyseal growth plates and stunted growth. Testosterone therapy may need to be decreased or stopped.
5. a. $MgSO_4$ can cause serious life-threatening cardiac rhythm changes and circulatory collapse. Therefore, continuous cardiac monitoring is the most important order to implement.
6. c. Given the context of a high school football player with these signs and symptoms, the nurse should recognize that the student may be misusing steroids. This question can help the nurse further assess the

situation.

7. d. Invasive dental procedures should not be planned during bisphosphonate therapy because of the high risk of developing bisphosphonate-induced osteonecrosis of the jaws (BIONJ).
8. a. Impaired liver function is a serious side effect of antiandrogen medications. Clients on bicalutamide have developed liver failure and died. Liver function must be monitored closely.
9. b. Bone density testing should be scheduled routinely to determine the effectiveness of the drug therapy.
10. a. In this case, the anabolic steroid would be used to improve health status, indicated by increased hemoglobin.

Chapter 37

Review Questions

1. a. The most important action for a nurse caring for transgender and nonbinary clients is to self-assess their own personal attitudes, beliefs, and feelings regarding these clients.
2. c. This is an intended effect of hormonal therapy for individuals undergoing MTF transition.
3. b. This is the only condition listed that is not a contraindication for testosterone therapy.
4. c. Hypertension is often treated with ACE inhibitors or angiotensin receptor blockers, which could cause hyperkalemia when given concomitantly with spironolactone.
5. b. Hyperkalemia is the most common and most serious adverse effect of spironolactone. Cardiac dysrhythmias and muscle cramps are indications of hyperkalemia and should be reported.
6. a. Finasteride is highly toxic to a fetus. Any female who is pregnant or of childbearing age should avoid contact with this medication, especially if the tablet is broken or crushed.
7. a. Testosterone therapy cannot be started in a pregnant client because of the dangers to the fetus.
8. b. A client transitioning from female to male who has not had gender-affirming surgery still has female organs and still needs regular screenings for cervical and breast cancer.
9. d. Spironolactone is an androgen blocker but does not block testosterone. Because the client is unsure about whether to transition, spironolactone is an appropriate choice because changes in sexual characteristics with spironolactone are reversible.
10. b. Androgens may decrease blood glucose levels; therefore, any hypoglycemic medication is likely to need a dosage adjustment.

Chapter 38

Review Questions

1. a. Gloves should be worn when handling this drug because it has the potential to cause cancer.
2. b. Erythromycin is the only FDA-approved eye medication used for ophthalmia neonatorum and is given directly after birth.
3. a. A “glaucoma suspect” has risk factors for glaucoma including elevated intraocular pressure, optic nerve damage, visual field deficit, or a strong family history of glaucoma.
4. d. Infections, such as eye infections, that are anatomically close to the brain can result in complications such as a secondary infection like meningitis.
5. c. Prostaglandin analogues cause hyperpigmentation of the eyelids and increase eyelash length and thickness.
6. b. Travoprost is more effective in Black clients than non-Black clients.
7. d. If the client does not apply pressure to the nasolacrimal area to reduce drainage of this beta-blocking ocular medication into the systemic circulation, a drop in heart rate can occur.
8. d. A known effect of prolonged ocular corticosteroids is an increased occurrence of cataracts.
9. a. Serious side effects of ocular antiviral medications include retinal detachment, which is manifested by floaters and flashes of light.
10. a. Because the drug is nonselective, it can bind to and block both beta-1 and beta-2 adrenergic receptors. When it binds to beta-2 receptors, it results in a decrease in heart rate, thus masking the signs of tachycardia often seen with hypoglycemia.

Chapter 39

Review Questions

1. b. The Eustachian tube connects the middle ear to the back of the nose and protects the middle ear from infection.
2. c. Decongestants such as pseudoephedrine may be given to relieve ear congestion and pressure.
3. d. Decreasing sodium intake can help reduce distracting sounds.
4. d. The client with a hearing impairment needs the nurse to be patient and provide them with time to communicate.
5. c. The client should avoid touching the tip of the dropper or inside of the cap with the hand or to any surface to avoid contamination.
6. c. Pain and ear itching are signs that a superinfection may be present, in which case an ear swab will be needed to test for a superinfection.
7. c. Diarrhea can develop with antibiotic use and should be reported to the provider.
8. c. Decongestants are known to elevate serum glucose.
9. b. The nurse should examine the ear canal to determine if the cerumen (earwax) has been expelled.
10. a. Ménière's disease is characterized by hearing loss, vertigo, increased sweating, nausea, and vomiting.

Chapter 40

Case Study

1. b. Red, scaling skin on the scalp and elbows and joint pain are findings consistent with psoriasis.
2. b. Coal tar is very damaging to unaffected skin and therefore should not be applied outside of the lesion borders. Zinc oxide or petrolatum should be used to protect the wound margins.

Review Questions

1. c. Adalimumab decreases the mitotic rate of skin cells to decrease scaling plaques in psoriasis.
2. a. Risks for embryo/fetal loss or abnormalities prevent the use of tretinoin during pregnancy.
3. c. Tetracycline drugs, when taken by children under the age of 8 years, may cause damage to bones and teeth; therefore, they are contraindicated in this population.
4. b. Psoriasis treatment requires exfoliation to remove plaque formation and drugs to decrease rapid skin cell growth to prevent plaques.
5. a. Covering topical steroids may cause both local irritation and systemic absorption of the drug.
6. d. Impetigo is a localized infection that requires treatment with antibiotics to eliminate the causative bacteria.
7. a. Acitretin is contraindicated in clients with decreased renal function.
8. a. Applying a nonocclusive dressing to protect the area is appropriate, but applying an occlusive dressing is contraindicated because it will increase the systemic effects of the medication.
9. c. With proper treatment, most forms of acne can be controlled with resolution or improvement in skin lesions.
10. c. Drinking alcoholic beverages when taking metronidazole results in a disulfiram-like reaction, which is evidenced by diaphoresis, hypotension, and nausea/vomiting.

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