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Seeley's

ESSENTIALS OF ANATOMY & PHYSIOLOGY

Cinnamon VanPutte • Jennifer Regan • Andrew Russo

McGraw Hill

Eleventh Edition

ELEVENTH EDITION

Seeley's Essentials of

Anatomy & Physiology

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Graw
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SEELEY'S ESSENTIALS OF ANATOMY & PHYSIOLOGY, ELEVENTH EDITION

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DEDICATION

This text is dedicated to our families. Without their uncompromising support and love, this effort would not have been possible. Our spouses and children have been more than patient while we've spent many nights at the computer surrounded by mountains of books. We also want to acknowledge and dedicate this edition to the previous authors as we continue the standard of excellence that they have set for so many years. For each of us, authoring this text is a culmination of our passion for teaching and represents an opportunity to pass knowledge on to students beyond our own classrooms; this has all been made possible by the support and mentorship we in turn have received from our teachers, colleagues, friends, and family.

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Courtesy of Bridget Reeves

Courtesy of the University of Iowa

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Cinnamon has been teaching biology and human anatomy and physiology for over two decades. At SIU School of Dental Medicine she teaches first year dental students and participates in dental-based physiology research. Cinnamon is an active member of several professional societies, including the Human Anatomy & Physiology Society (HAPS). Her Ph.D. in zoology, with an emphasis in endocrinology, is from Texas A&M University. She worked in Dr. Duncan MacKenzie's lab, where she was indoctrinated in the major principles of physiology and the importance of critical thinking. The critical thinking component of *Seeley's Essentials of Human Anatomy & Physiology* epitomizes Cinnamon's passion for the field of human anatomy and physiology; she is committed to maintaining this tradition of excellence. Cinnamon and her husband, Robb (also a biology professor), have two children: a daughter, Savannah, and a son, Ethan. Savannah is studying to become a child life specialist. Ethan is involved in 4-H and shows steers and lambs. He is pursuing his undergraduate education at Lindenwood University. Cinnamon and her family live on a farm with her parents, Tom and Bobbie, where they raise sheep and cattle.

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For over twenty years, Jennifer has taught introductory biology, human anatomy and physiology, and genetics at the university and community college level. She has received the Instructor of the Year Award at both the departmental and college level while teaching at USM. In addition, she has been recognized for her dedication to teaching by student organizations such as the Alliance for Graduate Education in Mississippi and Increasing Minority Access to Graduate Education. Jennifer has dedicated much of her career to improving lecture and laboratory instruction at her institutions. Critical thinking and lifelong learning are two characteristics Jennifer hopes to instill in her students. She appreciates the Seeley approach to learning and is excited about contributing to further development of the textbook. She received her Ph.D. in biology at the University of Houston, under the direction of Edwin H. Bryant and Lisa M. Meffert. She is an active member of several professional organizations, including the Human Anatomy and Physiology Society. Jennifer is married to Hobbie, a GIS supervisor. They have two sons, Patrick and Nicholas. Jennifer and Hobbie enjoy spending time on their small farm, tending the bees and the chickens, and their spoiled Boston Terrier, Sally.

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Andrew has over 20 years of classroom experience with human physiology, neurobiology, molecular biology, and cell biology courses at the University of Iowa. He is a recipient of the Collegiate Teaching Award and the J. P. Long Teaching Award in Basic Sciences. He is currently the course director for a new medical school course called Mechanisms of Health and Disease that integrates physiology, histology, and genetics. He is a member of several professional societies, including the Society for Neuroscience. Andrew received his Ph.D. in biochemistry from the University of California at Berkeley. His research interests are focused on the molecular basis of migraine. His decision to join the author team for *Seeley's Essentials of Human Anatomy & Physiology* is the culmination of a passion for teaching that began in graduate school. He is excited about the opportunity to hook students' interest in learning by presenting cutting-edge clinical and scientific advances. Andy is married to Maureen, a physical therapist, and has three daughters Erilynn, Becky, and Colleen, and six grandchildren. He enjoys all types of outdoor sports, especially bicycling, skiing, running, and open water swimming.

Preface

Seeley's Essentials of Anatomy & Physiology is designed to help students develop a solid, basic understanding of essential concepts in anatomy and physiology without an encyclopedic presentation of detail. Our goal as authors is to offer a textbook that provides enough information to allow students to understand basic concepts, and from that knowledge, make reasonable predictions and analyses. We have taken great care to select critically important information and present it in a way that maximizes understanding.

EMPHASIS ON CRITICAL THINKING

Critical thinking skills help students build a knowledge base for solving problems. An emphasis on critical thinking is integrated throughout this textbook. This approach is found in questions at the beginning of each chapter, and embedded within the narrative; in clinical material that is designed to bridge concepts explained in the text with real-life applications and scenarios; in Process Figure questions that apply physiological processes to practical situations, to promote applied understanding; in end-of-chapter questions that go beyond rote memorization; and in a visual program that presents material in understandable, relevant images.

- Pedagogy builds student comprehension from knowledge to application (Apply It questions, Critical Thinking questions, and Learn to Apply It Answers)

Apply It Questions challenge students to use their understanding of new concepts to solve a problem. Answers to the questions are provided at the end of the book, allowing students to evaluate their responses and to understand the logic used to arrive at the correct answer.

CRITICAL THINKING

1. An elderly male with normal vision developed cataracts. A surgeon treated his condition by removing the lenses of his eyes. What aspect of his vision will be most affected by the removal of the lenses? Explain your answer.
2. On a camping trip, Stephanie was admiring the stars in the night sky. She noticed a little cluster of dim stars at the edge of her vision, but when she looked directly at that part of the sky, she could not see the cluster. On the other hand, when she looked toward the stars but not directly at them, she could see them. Explain what was happening.
3. SCUBA divers are subject to increased pressure as they descend toward the bottom of the ocean. Sometimes this pressure can lead to damage to the ear and loss of hearing. Describe the normal mechanisms that adjust for changes in pressure. Explain how increased pressure might cause reduced hearing, and suggest at least one other common condition that might interfere with this pressure adjustment.
4. If a vibrating tuning fork were placed against the mastoid process of your temporal bone, you would perceive the vibrations as sound, even if the external auditory canal were plugged. Explain how this happens.
5. The main way that people "catch" colds is through their hands. After touching an object contaminated with the cold virus, the person transfers the virus to the nasal cavity, where it causes an infection. Other than the obvious entry of the virus through the nose, how could the virus get into the nasal cavity?

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Critical Thinking These innovative exercises encourage students to apply chapter concepts to solve a problem. Answering these questions helps students build a working knowledge of anatomy and physiology while developing reasoning skills. Answers are provided in Appendix D.

Clinical Emphasis—*Case Studies Bring Relevance to the Reader*

When problems in structure and/or function of the human body occur, this is often the best time to comprehend how the two are related. Clinical Impact boxes provide a thorough clinical education that fully supports the surrounding textual material. Systems Pathology boxes provide a modern and systems interaction approach to clinical study of the materials presented.

- Clinical Impact essays (placed at key points in the text)
- Chapter-opening clinical scenarios/vignettes
- Learn to Apply It and chapter Apply It questions with unique Learn to Apply It Answers
- Systems Pathology Boxes

CLINICAL IMPACT Color Blindness

Color blindness is the absence of perception of one or more colors (figure 9.17). Recall that color perception is the result of activation of different populations of cones. Color perception may be decreased or completely lost. The loss may involve perception of all three colors or of one or two colors. Most forms of color blindness occur more frequently in males and are X-linked genetic traits (see chapter 20). In Western Europe, about 8% of all males have some form of color blindness, whereas only about 1% of the females are color blind.

(a) (b)

Figure 9.17

These color blindness charts demonstrate the differences in color perception associated with some forms of color blindness. (a) A person with normal vision can see the number 74, whereas a person with red-green color blindness sees the number 21. (b) A person with normal vision can see the number 5. A person with red-green color blindness sees the number 2. (a) Steve Allen/Getty Images; (b) Prisma Bildagentur AG/Alamy Stock Photo

Reproduced from *Ishihara's Tests for Colour Deficiency* published by Kanehara Trading, Inc., Tokyo, Japan. Tests for color deficiency cannot be conducted with this material. For accurate testing, the original plates should be used.

Clinical Impact These in-depth essays explore relevant topics of clinical interest. Subjects covered include pathologies, current research, sports medicine, exercise physiology, pharmacology, and various clinical applications.

SYSTEMS PATHOLOGY

Stroke

Background Information

TABLE 8.9 REPRESENTATIVE DISEASES AND DISORDERS: Nervous System

Stroke

Symptoms

Treatment

SKELETAL

MUSCULAR

INTEGUMENTARY

ENDOCRINE

REPRODUCTIVE

CARDIOVASCULAR

URINARY

DIGESTIVE

RESPIRATORY

Figure 8.39 Ischemic Intracerebral Stroke

Figure 8.40 Brain Images of Stroke Victims

Systems Pathology Boxes These spreads explore a specific condition or disorder related to a particular body system. Presented in a simplified case-study format, each Systems

Pathology box begins with a patient history followed by background information about the featured topic.

MICROBES IN YOUR BODY How Bacteria Affect Cardiac Muscle

You've learned that the majority of bacteria are either harmless or an integral part of our well-being. Unfortunately, there are a handful of pathogenic bacteria that can interfere with the body's homeostasis.

Most people associate bacterial pneumonia with the lungs only. However, in the medical community, it is well known that pneumonia can cause serious heart problems. In fact, cardiac problems cause 70% of the deaths in individuals with other types of severe bacterial infections. Most bacterial pneumonia is caused by the bacterium *Streptococcus pneumoniae*, but until recently the mechanism by which this pathogen damages the heart had not been well understood. It seems that these bacteria induce the cells lining blood vessels to endocytose them and deposit them in cardiac muscle tissue. There, the bacteria release a toxin, called pneumolysin, which kills the cardiac muscle cells. These areas of dead cardiac muscle are called microlesions. In addition, during recovery from the infection, scars may form within the myocardium. Thus, the bacteria physically damage the heart, which interrupts the electrical signal necessary for cardiac muscle contraction. In addition, simply treating pneumonia with the traditional antibiotic, ampicillin, may actually worsen damage to the heart. Ampicillin causes the bacterial cell walls to burst, which releases a surge of pneumolysin, creating even more microlesions. Use of an antibiotic that does not destroy the bacterial cell walls will help reduce cardiac muscle death. Further, a vaccine against the bacterial molecule that induces the bacterial transport and against pneumolysin has shown great promise in minimizing the tissue damage caused by these bacteria.

Although pathogenic bacteria exist, modern medicine continues to make great strides to reduce their damaging effects on our bodies. In addition, the more we learn about our microbiome, the more effectively we may be able to prevent bacterial infections from occurring in the first place.

Understand **Apply It 4**

Given that Streptococcus pneumoniae microlesions interrupt the electrical activity that flows between cardiac muscle cells, the heart can experience severe stress and may malfunction or stop contracting altogether. Using what you learned about skeletal muscle contraction, would microlesions in skeletal muscle cause the same type of reaction as in cardiac muscle?

Microbes in Your Body helps students to understand the important role microbes play in helping various systems of the body to maintain homeostasis.

EFFECTS OF AGING ON THE LYMPHATIC SYSTEM AND IMMUNITY

Aging appears to have little effect on the lymphatic system's ability to remove fluid from tissues, absorb lipids from the digestive tract, or remove defective red blood cells from the blood. However, aging has a severe impact on the immune system.

With age, people eventually lose the ability to produce new, mature T cells in the thymus. By age 40, much of the thymus has been replaced with adipose tissue, and after age 60, the thymus decreases in size to the point that it can be difficult to detect. While the number of T cells remains stable in most individuals due to the replication (not maturation) of T cells in lymphatic tissues, the T cells are less functional. In many individuals, the ability of helper T cells to proliferate in response to antigens decreases. Thus, antigen exposure produces fewer helper T cells, which results in less stimulation of B cells and cytotoxic T cells. Consequently, both antibody-mediated immunity and cell-mediated immunity responses to antigens decrease with age.

Both primary and secondary antibody responses decrease with age. More antigen is required to produce a response, the response is slower, less antibody is produced, and fewer memory cells result. Thus, a person's ability to resist infections and develop immunity decreases.

The ability of cell-mediated immunity to resist intracellular pathogens also decreases with age. For example, the elderly are more susceptible to influenza (flu) and should be vaccinated every year. Some pathogens cause disease but are not eliminated from the body; with age, decreased immunity can lead to reactivation of the pathogen. An example is the virus that causes chickenpox in children, which can remain latent within nerve cells, even though the disease seems to have disappeared. Later in life, the virus can leave the nerve cells and infect skin cells, causing painful lesions known as herpes zoster, or shingles.

Autoimmune disease occurs when immune responses destroy otherwise healthy tissue. There is very little increase in the number of new-onset autoimmune diseases in the elderly. However, the chronic inflammation and immune responses that began earlier in life have a cumulative, damaging effect. Likewise, the increased incidence of cancer in the elderly is likely to be caused by a combination of repeated exposure to and damage from cancer-causing agents and decreased immunity.

Effects of Aging describes changes that occur as a person ages. Each reading focuses on the changes that occur in a specific body system.

Exceptional Art—*Instructive Artwork Promotes Interest and Clarifies Ideas*

A picture is worth a thousand words—especially when you're learning anatomy and physiology. Brilliantly rendered and carefully reviewed for accuracy and consistency, the precisely labeled illustrations and photos provide concrete, visual reinforcement of important topics discussed throughout the text.

Chapter-opener figures provide a visual overview of major concepts of the chapter, highlighting the components of systems, tissues, or mechanisms that will be explored.

Figure 7.16 APR **Muscles of Facial Expression and Mastication**

(a) Lateral view of facial muscles as seen from the right side. (b) Drawing and photograph of the anterior view of facial muscles. (b) McGraw Hill Education/ Photo and Dissection by Christine Eckel

Realistic Anatomical Art The anatomical figures in *Seeley's Essentials of Anatomy & Physiology* have been carefully drawn to convey realistic, three-dimensional detail. Richly textured bones and artfully shaded muscles, organs, and vessels lend a sense of realism to the figures that helps students envision the appearance of actual structures within the body.

Atlas-Quality Cadaver Images Clearly labeled photos of dissected human cadavers provide detailed views of anatomical structures, capturing the intangible characteristics of actual human anatomy that can be appreciated only when viewed in human specimens.

Figure 15.2 APR Nasal Cavity and Pharynx
(a) Sagittal section through the nasal cavity and pharynx. (b) Photograph of sagittal section of the nasal cavity. (b) Living Art Enterprises/Science Source

Multi-level Perspective Illustrations depicting complex structures or processes combine macroscopic and microscopic views to help students see the relationships between increasingly detailed drawings. Drawings are often paired with photographs to enhance the visualization of the structures.

Figure 10.15 APR Thyroid and Parathyroid Glands
(a) Anterior view of the thyroid gland. (b) The four small parathyroid glands are embedded in the posterior surface of the thyroid gland. (c) Three-dimensional interpretive drawing of thyroid follicles and parafollicular cells. (d) Light micrograph of thyroid and parathyroid tissue.
(d) ©Victor Eroschenko

Histology Micrographs Light micrographs, as well as scanning and transmission electron micrographs, are used in conjunction with illustrations to present a true picture of anatomy and physiology from the cellular level.

Specialized Figures Clarify Tough Concepts

Studying anatomy and physiology does not have to be an intimidating task mired in memorization. *Seeley's Essentials of Anatomy & Physiology* uses two special types of illustrations to help students not only learn the steps involved in specific processes, but also apply the knowledge as they predict outcomes in similar situations. Process Figures organize the key occurrences of physiological processes in an easy-to-follow format. Process Figure questions that follow each figure legend apply physiological processes to practical situations, to promote applied understanding. Homeostasis Figures summarize the mechanisms of homeostasis by diagramming how a given system regulates a parameter within a narrow range of values.

Step-by-Step Process Figures Process Figures break down physiological processes into a series of smaller steps, allowing readers to build their understanding by learning each important phase. Numbers are placed carefully in the art, permitting students to zero right in to where the action described in each step takes place.

Correlated with APR! Homeostasis Figures with in-art explanations and organ icons

- These specialized flowcharts illustrating the mechanisms that body systems employ to maintain homeostasis have been refined and improved in the ninth edition.
- More succinct explanations
- Small icon illustrations included in boxes depict the organ or structure being discussed.

Homeostasis Figure 18.17 Hormonal Regulation of Blood Volume and Its Effect on Urine Volume and Concentration

(1) Blood volume is in its normal range. (2) Blood volume increases outside the normal range, which causes homeostasis to be disturbed. (3) The control centers respond to the change in blood volume. (4) The control centers cause ADH and aldosterone secretion to decrease, which reduces water reabsorption. The control centers also cause dilation of renal arteries, which increases urine production. (5) These changes cause blood volume and thus blood pressure to decrease. (6) Blood volume returns to its normal range and homeostasis is restored. Observe the responses to a decrease in blood volume outside its normal range by following the red arrows.

Learn to Apply It and Learn to Apply It Answer—*Helping students learn how to think critically*

- A *Learn to Apply It* question begins each chapter, which links the chapter opener scenario and photo to the topics covered within the chapter. *Apply It* questions appear throughout each chapter, to reinforce critical thinking.

LEARN TO APPLY IT

Chase and Christina were studying for their last anatomy and physiology exam of the semester. After reviewing his notes on meiosis, Chase said, "Well, since meiosis is the same in males and females, I don't need to study the meiosis notes from the female reproductive system lecture." Christina quickly pointed out that he was mistaken and that if he reviewed his notes he would see that meiosis is very different in males and females.

After reading chapter 19, explain the major differences between meiosis in males and meiosis in females. Describe any advantages to the differences between male and female meiosis.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

- The answers to Learn to Apply It teach students step-by-step how to answer the chapter-opening critical thinking question. These answers to odd-numbered Apply It questions can be found in Appendix E. This is foundational to real learning and is a crucial part of helping students put facts together to reach that "Aha" moment of true comprehension.

Chapter 1

Learn to Apply It

The Learn to Apply It feature in every chapter of this text is designed to help you develop the skills to successfully answer critical thinking questions. The first step in the process is always to analyze the question itself. In this case, the question asks you to evaluate the mechanisms governing Renzo's blood sugar levels, and it provides the clue that there's a homeostatic mechanism involved. In addition, the question describes a series of events that helps create an explanation: Renzo doesn't feel satisfied after eating, has elevated blood sugar, and then is prescribed an insulin pump. In chapter 1, we learn that homeostasis is the maintenance of a relatively constant internal environment. Renzo experienced hunger despite eating, and his blood sugar levels were higher than normal. In this situation, we see a disruption in homeostasis because his blood sugar stayed too high after eating. Normally an increased blood sugar after a meal would return to the normal range due to the activity of insulin secreted by the pancreas. When blood sugar returns to normal, insulin secretion stops. In Renzo's case, his

cool water, the thermoreceptors would cause the hypothalamus to initiate shivering. Simply preventing sweating was insufficient to keep body temperature from dropping out of its normal range. If shivering continued to be ineffective, the body would conserve heat through loss of consciousness and severe hypothermia could set in.

3. In order to recognize which correct term to use here, you must first realize that directional terms are relative terms to the body. Therefore, it doesn't matter what position your body is in compared to the earth, body parts always have the same relationship to each other. Thus the nose is always referred to as being superior to the mouth.

5. The first step is to define the abdominopelvic and peritoneal cavities. The abdominopelvic cavity is located inferiorly to the diaphragm and superiorly to the pubic symphysis. The peritoneal cavity is located between the visceral peritoneum, which covers organs in the abdominopelvic cavity, and the parietal peritoneum, which lines the wall of

PEDAGOGICAL FEATURES ENSURE SUCCESS

Learning Outcomes are closely linked with in-chapter Apply It and Learn to Apply It questions as well as the Summary, Critical Thinking, and Review and Comprehension questions. These carefully designed learning aids assist students in reviewing chapter content, evaluating their grasp of key concepts, and utilizing what they've learned.

14.1 FUNCTIONS OF THE LYMPHATIC SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Describe the functions of the lymphatic system.
B. Explain how lymph is formed.

Studying Anatomy and Physiology does not have to be intimidating

Chapter Summary The summary is now conveniently linked by section and page number while it briefly states the important facts and concepts covered in each chapter.

SUMMARY

14.1 Functions of the Lymphatic System

The lymphatic system maintains fluid balance in tissues, absorbs lipids from the small intestine, and defends against pathogens.

14.2 Anatomy of the Lymphatic System

The lymphatic system consists of lymph, lymphocytes, lymphatic vessels, lymph nodes, tonsils, the spleen, and the thymus.

Lymphatic Capillaries and Vessels

1. Lymphatic vessels carry lymph away from tissues. Valves in the vessels ensure the one-way flow of lymph.
2. Skeletal muscle contraction, contraction of lymphatic vessel smooth muscle, and thoracic pressure changes move the lymph through the vessels.
3. The thoracic duct and right lymphatic duct empty lymph into the blood.

Lymphatic Organs

1. Lymphatic tissue produces lymphocytes when exposed to foreign substances, and it filters lymph and blood.
2. The tonsils protect the openings between the nasal and oral cavities and the pharynx.
3. Lymph nodes, located along lymphatic vessels, filter lymph.
4. The white pulp of the spleen responds to foreign substances in the blood, whereas the red pulp phagocytizes foreign substances and worn-out red blood cells. The spleen also functions as a reservoir for blood.
5. The thymus processes lymphocytes that move to other lymphatic

3. Macrophages are large phagocytic cells that are active in the latter part of an infection. Macrophages are positioned at sites where pathogens may enter tissues.
4. Basophils and mast cells promote inflammation. Eosinophils also play a role in inflammation associated with allergic reactions.
5. Natural killer cells lyse tumor cells and virus-infected cells.

Inflammatory Response

1. Chemical mediators cause vasodilation and increase vascular permeability, allowing chemicals to enter damaged tissues. Chemicals also attract phagocytes.
2. The amount of chemical mediators and phagocytes increases until the cause of the inflammation is destroyed. Then the tissues undergo repair.
3. Local inflammation produces redness, heat, swelling, pain, and loss of function. Symptoms of systemic inflammation include an increase in neutrophil numbers, fever, and shock.

14.5 Adaptive Immunity

1. Antigens are molecules that stimulate adaptive immunity.
2. B cells are responsible for antibody-mediated immunity; T cells are involved with cell-mediated immunity.

Origin and Development of Lymphocytes

1. B cells and T cells originate in red bone marrow. T cells are processed in the thymus, and B cells are processed in red bone marrow.
2. B cells and T cells move to lymphatic tissue from their processing sites. They continually circulate from one lymphatic tissue to

Remembering and Understanding These practice questions cover the main points presented in the chapter. Completing this self-test helps students gauge their mastery of the material.

REMEMBERING AND UNDERSTANDING

1. Define tissue and histology.
2. In what areas of the body is epithelium located? What are four characteristics of epithelial tissue?
3. Explain how epithelial tissue is classified according to the number of cell layers and the shape of the cells. What are pseudostratified columnar and transitional epithelium?
4. What kinds of functions does a single layer of epithelium perform? A stratified layer? Give an example of each.
5. Contrast the functions performed by squamous cells with those of cuboidal or columnar cells. Give an example of each.
6. What is the function of an epithelial free surface that is smooth? of one that has microvilli? of one that has cilia?
7. Name the ways in which epithelial cells may be connected to one another, and give the function for each way.
8. Define gland. Distinguish between an exocrine and an endocrine gland.
9. Explain the differences among connective tissue cells that are termed blast, cyte, and clast cells.
10. What are the functions of connective tissues?
11. What are the major connective tissue types? How are they used to classify connective tissue?
12. Describe areolar connective tissue, and give an example.
13. How is adipose tissue different from other connective tissues? List the functions of adipose tissue.
14. Describe dense collagenous connective tissue and dense elastic connective tissue, and give two examples of each.
15. Describe the components of cartilage. Give an example of hyaline cartilage, fibrocartilage, and elastic cartilage.
16. Describe the components of bone.
17. Describe the cell types and matrix of blood, and list the functions of blood.
18. Functionally, what is unique about muscle? Which of the muscle types is under voluntary control? What tasks does each type perform?
19. Functionally, what is unique about nervous tissue? What do neurons and glia accomplish? What is the difference between an axon and a dendrite?
20. Compare mucous and serous membranes according to the type of cavity they line and their secretions. Name the serous membranes associated with the lungs, heart, and abdominopelvic organs.
21. What is the function of the inflammatory response? Name the five symptoms of inflammation, and explain how each is produced.
22. Define tissue repair. What is the difference between regeneration and fibrosis?
23. Describe the process of tissue repair when the edges of a wound are close together versus when they are far apart.
24. Describe the effect of aging on cell division and the formation of

Critical Thinking Questions These innovative exercises encourage students to apply chapter concepts to solve problems. Answering these questions helps build their working knowledge of anatomy and physiology while developing reasoning and critical thinking skills.

CRITICAL THINKING

1. A patient is suffering from edema in the right lower limb. Explain why elevation and massage of the limb help remove the excess fluid.
2. If the thymus of an experimental animal is removed immediately following birth, the animal exhibits the following characteristics:
   a. increased susceptibility to infections
   b. decreased numbers of lymphocytes
   c. greatly decreased ability to reject grafts

   Explain these observations.
3. Adjuvants are substances that slow, but do not stop, the release of an antigen from an injection site into the blood. Suppose injection A of a given amount of antigen is given without an adjuvant and injection B of the same amount of antigen is given with an adjuvant that caused the release of antigen over a period of 2 to 3 weeks. Does injection A or injection B result in the greater amount of antibody production? Explain.

Chapter-by-Chapter Changes

Global Changes

- Added Chapter 0, a student study resource guide with text-specific figure symbols and format guide
- Added figures spanning two pages that tie together multiple steps of a single process or several ideas into one complete figure
- Increased vibrancy, clarity, and vividness of colors in the art program
- Descriptions of process figure events are now within the text with a bullet linking the text to the corresponding portion of the figure to help the student better follow the text
- Gender-neutral language throughout with use of biological sex pronouns throughout the entire book
- Bloom's levels were added to all in-text questions
- Word pronunciations guides have all been converted to the phonetic pronunciation rather than symbols
- Throughout, numbering has been added to lists of terms to help reduce cognitive load for the student

Chapter 1

- Added a situational process figure to illustrate negative and positive feedback
- Figure 1.8 updated to include the gallbladder
- Definition of "variable" within homeostasis discussion has been updated to be more accurate

- Added an analogy to illustrate the importance of body temperature maintenance
- Modified the definition of positive feedback to be more clear
- Reorganized the discussion of positive feedback to flow more logically
- Updated the definition of etymology for clarity
- Reworded the definition of ventral and dorsal to be more clear
- Reorganized section on body cavities to include dorsal body cavity, a term commonly used within the allied health fields
- Reorganized the body membranes section to flow more logically
- Integrated clinical information into the body cavities section

Chapter 2

- Added a figure demonstrating the relationship between electronegativity and bond formation (fig 2.2)
- Added figures demonstrating electron distribution between atoms, depending on bond type (figs 2.4 and 2.5)
- Added figure depicting electron position within a molecule with polar bonds (2.5)
- Added figure demonstrating the relationship between pH and H^+ and the connection to household items (fig 2.10)
- Figure 2.11 on buffers has been revised for clarity
- Added definition of an “electron cloud”
- Per a reviewer’s suggestion, added definition of isotope
- Updated the definition of ionic bonding for clarity
- Simplified the discussion of chemical bonds by integrating a stepwise association with the corresponding process figure; it is now more logical
- Rearranged the order of the discussion of energy for simplicity and clarity

- Added the definition of “gene” to nucleic acid discussion

Chapter 3

- New chapter-opener figure
- New figure 3.1 highlighting the components of a cell
- Added headings to distinguish between passive membrane transport processes and active membrane transport processes
- Description of transcytosis added

Chapter 4

- Revised tables that list tissue types to make it easy to compare one tissue to another tissue
- Added two 2-page figures illustrating the distribution of epithelial and connective tissues throughout the body
- Updated the description of epithelial tissue for clarity
- Changed the descriptions of the epithelial tissue types to be more succinct
- Reorganized the discussion of epithelial tissue types to be more logical
- Reorganized the discussion of secretory glands for logic and clarity
- Added a table organizing gland type by structure and mode of secretion
- Per reviewer suggestion, added a new Apply It question to the muscle tissue section
- Reorganized the discussion of inflammation to correspond with the accompanying process figure
- Reorganized the discussion of tissue repair to correspond with the accompanying process figure

Chapter 5

- New chapter-opener figure
- List of five epidermal strata added
- Description of thick skin versus thin skin added
  Page xvi
- Added term *friction ridge* and explained its relationship to fingerprints
- Added explanation of why different types of injections are used
- Description of fourth-degree burns added

Chapter 6

- Added a figure illustrating the anatomy of spongy bone
- Updated the figure depicting the process of intramembranous ossification for clarity
- Updated the figure depicting the process of endochondral ossification to include a timeline for when each event occurs
- Updated the figure of the overview of skeletal anatomy to visually differentiate between axial skeleton and appendicular skeleton
- Added a figure of the superior view of the skull for better visualization of skull sutures
- Updated multiple figures throughout the chapter to have more distinct detail and more vivid coloration
- Revised the introduction to bone matrix section to better illustrate the relationship between form and function, with a reference to chapter 4
- Reorganized the order of chapter sections for more logical flow

- Added a new figure comparing the three bone-cell types
- Rewrote the section on bone histology to clarify the function of each bone cell
- Reorganized the section on bone development to correlate with the process figures
- Reorganized the section on bone repair to correlate with the process figure
- Rewrote the section on Ca^{2+} homeostasis to flow more logically and to be more clear
- Replaced figure 6.10 with a homeostasis figure to simplify the visual representation of Ca^{2+} homeostasis
- The skull bone anatomy has been rearranged to be organized by bone rather than by view of skull to streamline this information and reduce redundancy
- The section on appendicular bone anatomy has been reorganized by girdle, then by bone
- The section on joints has been reorganized to be more logical

Chapter 7

- The art has been updated to be more vivid and realistic
- The physiology art is reorganized with new figures that help the students keep track of what portion of the process they learning and how it relates to the other steps in the sequence as well as the location within the cell
- Updated the figure illustrating energy sources for muscle contraction to be more streamlined and logical
- Reorganized section 7.3 on skeletal muscle anatomy to be more logical and to be more clear
- Added an organizing principle to skeletal muscle fiber anatomy and its role in muscle contraction
- Added a figure illustrating the resting membrane potential

- Reorganized the section on action potentials to correlate with the corresponding process figure
- Reorganized the section on the neuromuscular junction to correlate with the corresponding process figure
- Rewrote the portion of this section that describes the link between the action potential and muscle shortening
- Incorporated an active learning tip for the cross-bridge cycle
- Rewrote the portion of this section describing the cross-bridge cycle to correlate with the corresponding process figure
- Reorganized the section on whole-muscle physiology to flow more logically
- The term *recovery oxygen consumption* is replaced with *excess post-exercise consumption*
- Updated the section on energy sources for contraction to reflect more current terminology
- Added a study tip for approaching the learning of skeletal muscle anatomy
- Reorganized the anatomy section to include more separate sections of muscles for clarity
- Updated the description of the pelvis diaphragm for accuracy

Chapter 8

- New chapter-opener figure
- New figure representing the organization of the nervous system
- Added description of satellite cells in the discussion of PNS glial cells
- Revised the section “Resting Membrane Potential” for clarity

- New figure highlighting the phase of nerve cell communication: stimulation of action potential, action potential propagation, and synaptic communication
- Added active learning prompts (action potential propagation)
- Moved the description of reflexes to discussion of spinal cord to eliminate redundancy
- Changed to “dorsal” and “ventral” in reference to horns in spinal segment description
  Page xvii
- Statement added about the function of the insula (taste perception)
- Replaced the term “primary somatic sensory cortex” with the term “primary somatosensory cortex”

Chapter 9

- New chapter-opener figure
- Additional information concerning proprioception and the righting reflex added
- Section on “Pain” revised for clarity
- Description of photoreceptor function moved to the section “Function of the Eye” so that physiological processes are grouped together
- New figure highlighting the process of vision added

Chapter 10

- Added a figure comparing transport of water-soluble hormones to lipid-soluble hormones
- Updated figure 10.3 for clarity
- Updated figure 10.10 for clarity

- Updated the discussion of binding proteins to be more clear
- Rewrote the section on water-soluble hormone transport to be more logical
- Reorganized the discussion of control of hormone secretion to correlate with the corresponding process figure
- Deleted figure 10.9 and incorporated some of that information into figure 10.10 to be clearer and less visually detailed
- Updated information on prolactin-inhibiting hormone for accuracy
- Reorganized the discussion on the adrenal cortex to be more logical
- Deleted figure 10.20 to be more in line with the level of detail throughout the chapter; this topic is discussed further in chapter 18

Chapter 11

- New chapter-opener figure
- Updated description of red blood cell structure to accurately relate to function
- Updated figure 11.2 to reflect level of detail in the text
- New figure of life history of red blood cell added
- Revised figure detailing the breakdown of hemoglobin for clarity
- New figure illustrating blood typing added

Chapter 12

- New chapter-opener figure
- New two-page figure highlighting the Cardiac Cycle

- Section 12.5, “Stimulation of the Heart,” has been updated with a introduction to prepare students for the detailed description of action potentials and cardiac muscle activity
- Panel labels have been added to figure 12.19, Events of the Cardiac Cycle, to correlate with references in the text, which will help the reader interpret the multiple graphs
- Clear descriptions of extrinsic regulation and intrinsic regulation added to the introduction of section 12.8, “Regulation of Cardiac Function”

Chapter 13

- New chapter-opener figure
- Figure 13.24 revised for clarity
- New figure 13.21 summarizes the regulation of blood flow

Chapter 14

- New chapter-opener figure
- New figure 14.8 summarizes the components of immunity
- Revised description of specificity in section 14.3 for clarity
- Revised description of self antigen for accuracy
- Revised the section “Antigen Recognition” for accuracy and clarity
- Figure 14.11 revised to include memory helper T cells

Chapter 15

- This chapter has been completely reorganized and rewritten for more coherent flow of information
- The discussion of ventilation and gas laws has been combined

- Organized the physiology discussion into respiration versus gas transport with a separate section on metabolic factors affecting gas transport
- Figure 15.13 was updated to depict O_2 molecules bound to the hemoglobin molecule
- Added an overview figure of CO_2 transport mechanisms

Chapter 16

- Rearranged figure 16.9 to better illustrate each of the three phases of swallowing
- Added a part (e) to figure 16.11 to illustrate the specific location of nutrient absorption
- Updated figure 16.23 to include images of the nutrient molecules
- Updated figure 16.24 with a better representation of digestive actions in each region of the digestive tract
- Updated figures 16.25 and 16.26 to be more realistic
- Updated the anatomy description of the stomach to be more clear
  Page xviii
- Reorganized the text in section 16.4 to correlate with the corresponding process figure
- Rewrote the anatomy description of the liver to better illustrate the relationships among its components
- Rewrote the description of bile to be more clear
- Reorganized the section on functions of the liver to correlate with the corresponding figure
- Rewrote the section on the anatomy of the pancreas to be more clear
- Rewrote the section on the defecation reflex to be more coherent

Chapter 17

- New chapter-opener figure
- New figure 17.4 illustrates the pathways of macromolecule breakdown for ATP production
- Updated the numbers of ATP produced from glucose metabolism

Chapter 18

- Added a figure depicting urine flow through the urinary system (figure 18.4)
- Added a flowchart depicting blood flow through the kidney (figure 18.7)
- Edited figure 18.8 to show the urine formation process with a more realistic relationship to the nephron
- Figure 18.9 was revised to be clearer and to link to other corpuscle images
- Figure 18.10 was revised as a two-page spread highlighting the reabsorption of solutes and water
- Figure 18.13 was recast as a two-page spread to illustrate water conservation and filtrate flow
- Figure 18.15 was edited to include details of the collecting duct
- Per reviewer request, a photomicrograph of transitional epithelium was added to figure 18.18
- Per reviewer request, figure 18.20 as added to review the principles of osmosis
- Rewrote the section on urine flow to correspond to the new portion of figure 18.4
- Throughout the chapter, the text was reorganized to correlate with the corresponding process figures

- Per reviewer request, added a discussion of countercurrent mechanism to help provide context for the ability of the kidney to conserve water
- Rewrote the section on renin-angiotensin-aldosterone to be more logical
- Rewrote the section on intracellular fluid compartments and extracellular fluid compartments
- Rewrote the section on Na^+ regulation for clarity
- Rewrote the section on Ca^{2+} homeostasis to be clearer
- Simplified the section on buffers

Chapter 19

- Figure 19.5 revised as a two-page figure outlining the process of spermatogenesis
- Figure 19.11 revised as a two-page figure outlining the maturation of the oocyte and follicle
- Rewrote the section on meiosis to be clearer
- Meiosis discussion now correlates with the corresponding process figure
- Added a new Clinical Impact box, “Gender and Sex,” introducing the concept of the difference between biological sex and gender identity
- Rewrote the section on the anatomy of the scrotum to clarify the relationship between temperature and sperm development
- Rewrote the text on spermatogenesis to correlate with the corresponding process figure
- Used biological sex terms rather than gender terms throughout the chapter
- Rewrote the section on infertility in males for clarity
- Integrated the discussion on follicle development and oocyte development to reduce redundancy

- Revised the statement on the length of the menstrual cycle to be more general
- Updated the section on birth control to be more current

Chapter 20

- New chapter-opener figure
- Introduction to section 20.1, “Prenatal Development,” revised to include list of prenatal and postnatal life stages
- Discussions of neural tube and neural crest formation revised for clarity
- Description of formation of the heart revised to better reflect the detail in figure 20.13

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Acknowledgments

In today's world, no textbook is brought to fruition through the work of the authors alone. Without the support of friends, family, and colleagues, it would not have been possible for us to complete our work on this text. The final product is truly a team effort. We want to express sincere gratitude to the staff of McGraw Hill for their help and encouragement. We sincerely appreciate Senior Portfolio Manager Matt Garcia and Product Developer Melisa Seegmiller for their hours of work, suggestions, patience, and undying encouragement. We also thank Content Project Manager Ann Courtney, Content Licensing Specialist Lori Hancock, Buyer Laura Fuller, and Designer David Hash for their hours spent turning a manuscript into a book; Assessment Project Manager Brent dela Cruz for his assistance in building the various products that support our text; and Marketing Manager Valerie Kramer for her enthusiasm in promoting this book. The McGraw Hill LLC employees with whom we have worked are extremely professional, but more than that, they are completely dedicated to their role as part of the content team.

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CHAPTER

0

How to Be Successful in A&P

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Hello, Students! Author Cinnamon VanPutte would like to share something with you: she failed her college organic chemistry course. Later, she retook it and earned an "A." Why does this matter to you? We hope this helps you

understand that your authors have been there. Yes, we've earned an "A" in hard classes—but we also know what it is to struggle in a class. We've had to retool our study habits; we've had to learn how to effectively use a textbook. These experiences have helped inform our approach to this textbook, and we hope this helps you. We know that many of you will sail right through A&P and would have done so even without reading this success guide, while others may be retaking A&P for the second or third time. By taking the time to read this guide, you have already taken a positive first step to being able to succeed in A&P. You have entered a partnership with your instructor and us, the authors. If you utilize the tips, techniques, and information that we, as well as your instructors, are providing to you, we know you will learn a lot of information and you will be positioned to succeed in this course.

0.1 THE WORLD OF A&P

If you search online for "hardest classes in college," A&P will show up on many lists. But don't worry! We are here to help! We have each taught A&P for more than 20 years and have seen countless students, who were very nervous on the first day, successfully move through the course—all the while gaining self-assurance, confidence, and a deep understanding of the fundamental concepts needed to perform well in the course.

The study of A&P entails a lot of information. Depending on the particular course, the first semester of A&P may start with a discussion of matter and chemical bonds, and end with the complexities of the nervous system (such as action potentials). Truthfully, this means progressing from introductory material to more advanced material within a single semester.

In addition, you will be learning the vocabulary of A&P, which means you are essentially learning a foreign language—you might even feel like you're learning more new vocabulary than if you were actually learning a foreign language! In an effort to make this task easier, our textbook provides phonetic pronunciations of these vocabulary terms, similar to those found on Facebook for people's names. For example, the gluteus maximus pronunciation would be: GLOO-tee-us MAX-ih-mus. We think this type of guide will help you learn the terminology very readily and be more confident speaking the language—if you can say it out loud, then you can probably spell it and are better poised to remember it.

It's also important to realize that the information in A&P cannot be effectively understood through memorization alone. Much of the physiology material requires that you use critical thinking skills. Many of you may be planning careers in science or health professions, such as nursing or pharmacy—professions in which the ability to problem solve is essential. In

this book we will help you develop critical thinking skills and thus a deep understanding of complex concepts.

0.2 DEVELOPING CRITICAL THINKING SKILLS

So, what is required to develop critical thinking skills? What even are critical thinking skills? To understand these questions, we need to explore the difference between simple memorization—what you may have always called "studying"—and **conceptual learning**. Many of you have enjoyed much success in high school and in some of your early introductory-level college classes through "studying." However, to be successful in most A&P classes, you will also need to develop skills for conceptual learning. The basis for this difference is best described using Bloom's taxonomy, originally published by B. Bloom and colleagues in 1956. Over time, Bloom's taxonomy has been modified and can be best thought of as a model for the gradual increase in the amount of abstract thought required to achieve a particular level of learning. The simplest, most concrete level of learning is *remembering*, or simply memorizing. As you climb the levels of Bloom's, your ability to put ideas into your own words (*understanding*) and then to solve problems you've never seen before (*applying*) increases. Thus, as you gain these skills, you are now *learning* the material and can answer **how** and **why** a particular process happens, and you can predict outcomes to unfamiliar scenarios. This textbook will guide you in developing those skills.

To do this, you will begin to use **metacognition** in your learning. Metacognition was first defined by Flavell in 1976 as "thinking about your own thinking"—in other words, deciding whether you truly understand and can apply fundamental physiological and anatomical principles. We are going to provide you with five metacognitive learning strategies to ensure your success in A&P.

0.3 FIVE METACOGNITIVE LEARNING STRATEGIES

What will you need to do to achieve the goal of being successful in A&P? There are five specific tasks you can employ to be successful in A&P. These tasks are adapted from the book *Teach Students How to Learn* by S. Y. McGuire. They are the following:

1. Attend every class session and take notes with a pen and paper.
2. Read, read, read!
3. Work with other students.
4. Do homework as if it were the test.
5. Engage in concentrated study sessions.

We will address each of these tasks in the remainder of this success guide with specific information on how to use this textbook.

0.4 USING THE FIVE METACOGNITIVE LEARNING STRATEGIES WITH THIS TEXTBOOK

1. *Attendance and Note-Taking*. It is essential that you attend each class session. As you can see, this book has 20 chapters, each of which covers a topic for which you could take an entire semester class, or more! Your instructor will decide what material they will cover. Some instructors may expect you to glean specific information directly from the book. Therefore, to make sure you hear, firsthand, all the information and messages your instructor presents in class, it is critical you be in class. Then, while in class, take notes by hand! Students who handwrite their notes outperform students who take notes with their laptops. The difference is that taking notes by hand requires you to use your own words, which helps you remember the information better. After the class session, it is also helpful to take notes by hand directly from the assigned chapters.
2. *Read, Read, Read!* Possibly one of the biggest misconceptions regarding reading a textbook is that it is no different from reading a novel—which couldn't be farther from the truth. Reading a science textbook involves a slow and systematic process. There are three types of reading strategies you'll need to employ to get the most information from each chapter: (1) preview, (2) prepare for active reading, (3) actively read.
   a. Preview
   Previewing a chapter is like watching a movie trailer or reading the description of a book to see what it's about and whether it interests you. Skim the section headings. Each system chapter of this textbook is laid out in the following way:
   - Anatomy of the System
     - Organs
     - Histology
   - Functions of the System
     - Major Functions
     - Integration of Functions for Homeostasis

   Some sections are further subdivided into specialized topics to walk you through a process step-by-step.

   While you're previewing the chapter, pay attention to bolded terms, phonetic pronunciations, and word origins. Root words tell a lot of

information about a process or structure; for example, *hyper-* indicates higher or above, and *hypo-* indicates lower or below, and they are used both anatomically and physiologically.

b. Prepare for Active Reading
As you're previewing, or as a next step, write out questions you'd like answered as you read. The bold terms can be used as a guide to the questions.

c. Actively Read
After you've previewed the chapter and have done the preparations for active reading, the next step is to actively read. This can be done one paragraph, or one concept in SmartBook 2.0, at a time. Write notes in your own words as you read. Add a paragraph, or concept, at a time, all the while adding ideas from the previous paragraph. In this way, you're "taking one bite at a time" of the chapter's information. This helps your brain integrate information and keeps it from suffering information overload. As you actively read, there are several features that are consistent throughout this text that can serve as guideposts for you. We present these features in the section "Textbook Features and Figure Colors and Symbols."

3. *Work with Other Students Enrolled in the Same Class.* Author C. VanPutte would like to share something else with you: she did not fully comprehend the concept of osmosis until she taught her first college-level class. Once she had to explain the concept out loud and in her own words, a light clicked on! So, form study groups! Assign each other topics on which to lecture to the group. Write practice exams for each other. Sometimes your peers can help you as much as, or perhaps more than, the instructor.

4. *Do Homework as if It Were the Test.* For most lecture exams you will not be allowed to use your notes, the textbook, or the internet. So you need to practice for that situation. Don't simply copy answers onto your homework assignments. Instead, study first, then do the homework without assistance. Then, if you get stuck, use your resources. For example, you could do a "recharge" in SmartBook 2.0, or visit your instructor during their office hours.

5. *Utilize Multiple, Intense, Short Study Sessions.* Our brains work more efficiently when we stay focused for a relatively brief period of time: approximately 30–50 minutes. Staring blankly at your notes for 3 hours is not helpful. Therefore, decide what you're going to focus on, then study with intent for 30–50 minutes. Studying with intent involves actively engaging with the material. This can include making a concept map, expanding on your notes and rephrasing them, writing out a summary and simply thinking about the material. Take a short 10- to 15-minute break, then briefly review what you just studied. Do this 3–5 times a day for each class in which you're enrolled.

0.5 TEXTBOOK FEATURES AND FIGURE COLORS AND SYMBOLS

Throughout this textbook you will see certain repeating features and symbols. These symbols are always a particular color; however, for our students with vision disabilities, these colored symbols are also uniquely labeled.

1. In-Text Numbering
   As you're reading, look for areas where we've tried to make complex topics clearer by numbering steps or components. This ensures that you don't miss a step or a part.

> In an unstimulated cell, this charge difference is called the **resting membrane potential**. Although we call it the resting membrane potential, the cell is more like a sprinter in starting blocks; it is ready to respond at a moment's notice. The resting membrane potential is the result of three factors: (1) The concentration of K^+ inside the cell membrane is higher than that outside the cell membrane, (2) the concentration of Na^+ outside the cell membrane is higher than that inside the cell membrane, and (3) the cell membrane is more permeable to K^+ than to Na^+.

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2. Process Figures
   For complex processes, we have process figures that break down the step-by-step sequence of events. The in-text explanations directly correlate to portions of the figure by the use of purple circle numbers.

3. Side-by-Side Anatomy Figures

In certain anatomy figures, we have placed a photograph next to an artistic rendering. This allows for accurate interpretation of artist-generated figures.

McGraw Hill Education/Photo and Dissection by Christine Eckel

4. Homeostasis Figures
   These figures walk you through certain critical physiological mechanisms involved in the maintenance of homeostasis. Icons depict the particular organs discussed, in order to help strengthen associations between anatomy and physiology.

5. Clinical Content
   a. Clinical Impact: explore interesting clinical aspects of the body system being discussed

CLINICAL IMPACT Gender and Sex

At birth, people are assigned one of three biological sexes based solely on the anatomy of their external genitalia. Males have a penis, females have a vagina, and intersex people can have a wide variation in sexual characteristics. However, anatomy does not always dictate a person's gender identity. Gender identity is how people view and express themselves in the world. Biological sex also does not determine a person's sexual orientation. Sexual orientation is the interpersonal interactions people have with others with regard to physical, emotional, and romantic attraction. Sexual orientation also does not determine sexual preference. Sexual preference refers to the way a person wishes to receive and participate in physically intimate actions.

Until about the 1990s, the societal norm for humans in the United States consisted of a gender binary. The gender binary is the system of viewing gender as consisting of only two identities and two sexes: male and female. However, since the 1990s, it has been recognized that gender exists along a gender spectrum, sometimes referred to as nonbinary. The gender spectrum is a continuum of gender identity that includes male and female, but does not assert male and female as absolutes or as polar opposites.

For parents of a gender-expansive child, one who goes against societal norms for gender identity, the first source of information is usually a medical professional. This means that physicians, nurses, and all medical professionals are put into a pivotal role of helping to provide understanding and resources to parents.

An immense set of terms exists to describe gender identity, sexual orientation, and sexual preference. Here, we provide a brief introduction to some of these terms:

1. Gender identity—how individuals view themselves; gender identity can be the same or different than the sex assigned to them at birth.
2. Gender expression—how individuals present themselves in terms of appearance, behavior, clothing, haircut, etc.
3. Gender nonconforming—behaving in a way that does not conform to societal expectation of biological sex
4. Queer—a previously derogatory term used for certain sexual orientations, but now is used to express fluid identities and orientations; usually used by people who do not identify as straight (heterosexual)
5. Transgender—individuals whose gender identity and/or gender expression is not the same as societal expectations based on their assigned biological sex. Although this does not imply a particular sexual orientation, it can be described as an FtM (F2M), female to male, transition or an MtF (M2F), a male to female, transition when individuals begin to express the knowledge of their internal identity by their outward appearance.
6. Gender dysphoria—the term used to describe the long-term distress individuals experience when their assigned biological sex does not align with their gender identity
7. Gay—the sexual attraction and affectional orientation between members of the same gender (assigned or expressed); refers to males and females
8. Pansexual—not limited in attraction to an individual with regard to biological sex, gender, or gender identity
9. Lesbian—the sexual attraction and affectional orientation between two females (assigned or expressed)
10. Bisexual—being sexually, emotionally, and physically attracted to people of both the same gender and another gender

b. Microbes in Your Body: highlight the role of microbes in maintaining homeostasis

MICROBES IN YOUR BODY Hormonal Regulation of Nutrient Metabolism is Influenced by Gut Microbes

Obesity has increased at an alarming rate over the last three decades. It is estimated that over 150 billion adults worldwide are overweight or obese. In the United States, 1/3 of adults are obese. As obesity rates have increased, so have the rates of obesity-related health conditions such as insulin resistance, diabetes, and cardiovascular disease. Why this dramatic increase? There are two main reasons for obesity: diet/lifestyle and gut bacteria; it seems these two may be related.

The most familiar cause of obesity is diet and lifestyle. The "typical" Western diet consists of frequent large meals high in refined grains, red meat, saturated fats, and sugary drinks. Combined with a reduction in physical activity and less sleep for many Americans, the Western diet and lifestyle can lead to obesity and poor health.

However, could humans' gut microbiota be just as responsible (or even more responsible) for obesity? Comparisons between the gut microbiota of lean versus obese individuals seem to suggest the possibility of an important link between gut microbiota and our weight. The human gut, like other animals, is densely populated with microbiota. The majority (90%) of human gut bacteria fall into two groups: Firmicutes and Bacteroidetes. Lean people have more Bacteroidetes than Firmicutes, while the opposite is true for obese people.

We now know that gut microbiota affect nutrient processing and absorption, hormonal regulation of nutrient use by body cells, and even our hunger level.

Changes in gut microbiota alter the hormonal regulation of nutrient use. Inflammation-promoting effects of an imbalanced gut microbiota is thought to induce obesity via promoting insulin resistance, a known autoimmune malfunction. Normal gut microbiota metabolism is critical for secretion of several anti-hunger hormones, and anti-depressive neurotransmitters and neurochemicals. Shifts in normal gut microbiota, as related to diet, may very well disrupt normal anti-hunger signals and gut permeability, leading to over-eating and inflammation related to obesity.

Can gut microbiota in obese people be manipulated to cause them to become lean? Several possibilities exist, including the distinct possibility that prescribing antibiotics against bacteria associated with obesity could shift the metabolism of an obese person to become leaner. Another possibility is the use of prebiotics—nondigestible sugars that enhance the growth of beneficial microbiota. Finally, probiotic use is another possible intervention for obesity. Probiotics are nonpathogenic live bacteria that confer a health benefit to the host. This is a rapidly expanding field that holds much promise, but it is still in its beginning stages of our understanding.

c. Aging: describe changes to the body systems as we age

EFFECTS OF AGING ON THE ENDOCRINE SYSTEM

Age-related changes to the endocrine system include a gradual decrease in the secretion of some, but not all, endocrine glands. Some of the decreases in secretion may be due to the fact that older people commonly engage in less physical activity.

GH secretion decreases as people age. However, regular exercise offsets this decline. Older people who do not exercise have significantly lower GH levels than older people who exercise regularly. Decreasing GH levels may explain the gradual decrease in bone and muscle mass and the increase in adipose tissue seen in many elderly people. So far, administering GH to slow or prevent the consequences of aging has not been found to be effective, and unwanted side effects are possible.

A decrease in melatonin secretion may influence age-related changes in sleep patterns, as well as the decreased secretion of some hormones, such as GH and testosterone.

The secretion of thyroid hormones decreases slightly with age. Age-related damage to the thyroid gland by the immune system can occur. Approximately 10% of elderly women experience some reduction in thyroid hormone secretion; this tendency is less common in men.

The kidneys of the elderly secrete less renin, reducing the ability to respond to decreases in blood pressure.

Reproductive hormone secretion gradually declines in elderly men, and women experience menopause (see chapter 19).

Secretion of thymosin from the thymus decreases with age. Fewer functional lymphocytes are produced, and the immune system becomes less effective in protecting the body against infections and cancer.

Parathyroid hormone secretion increases to maintain blood calcium levels if dietary Ca^{2+} and vitamin D levels decrease, as they often do in the elderly. Consequently, a substantial decrease in bone matrix may occur.

In most people, the ability to regulate blood glucose does not decrease with age. However, there is an age-related tendency to develop type 2 diabetes mellitus for those who have a familial tendency, and it is correlated with age-related increases in body weight.

d. Systems Pathologies: discuss a disorder or disruption in a particular body system

SYSTEMS PATHOLOGY

Burns

Background Information

Sam is a 23-year-old male who fell asleep while smoking. His burning cigarette started a fire. Burns can damage the body in many ways (figure 5.11). Sam received partial-thickness and full-thickness burns to his face, arms, upper torso, and legs (figure 5.12). When large areas of skin are severely burned, the resulting systemic effects can be life-threatening. Within minutes of a major burn injury, there is increased permeability of small blood vessels called capillaries. This increased permeability occurs at the burn site and throughout the body. As a result, fluid and ions are lost from the burn wound and into tissue spaces. The loss of fluid decreases blood volume, which decreases the heart's ability to pump blood. The resulting decrease in blood delivery to tissues can cause tissue damage, shock, and even death. Treatment consists of administering intravenous fluid at a faster rate than it leaks out of the capillaries. Although this fluid replacement can reverse the shock and prevent death, fluid continues to leak into tissue spaces, causing pronounced edema (swelling). Typically, after 24 hours, capillary permeability returns to normal, and the amount of intravenous fluid administered can be greatly decreased.

Substances released from the burn may also play a role in causing cells to function abnormally. Burn injuries result in an almost immediate hypermetabolic state, resulting from an increase in body temperature and changes in hormone secretion. Compared with a normal body temperature of approximately 37°C (98.6°F), a typical burn patient may have a body temperature of 38.5°C (101.3°F), despite the higher loss of water by evaporation from the burn.

In severe burns, the increased metabolic rate can result in loss of as much as 30–40% of the patient's preburn weight. To help compensate, treatment may include doubling or tripling the patient's caloric intake. In addition, the need for protein, which is necessary for tissue repair, is greater.

Normal skin maintains homeostasis by preventing microorganisms from entering the body. Because burns damage and sometimes completely destroy the skin, microorganisms can cause infections. For this reason, burn patients are maintained in an aseptic (sterile) environment (figure 5.13), which attempts to prevent the entry of microorganisms into the wound. They are also given antimicrobial drugs, which kill microorganisms or suppress their growth. Debridement (deh-BREED-mentl), the removal of dead tissue from the burn, helps prevent infections by cleaning the wound and removing tissue in which infections could develop. Skin grafts, performed within a week of the injury, also help close the wound and prevent the entry of microorganisms.

Despite these efforts, however, infections are still the major cause of death for burn victims. Depression of the immune system during the first or second week after the injury contributes to the high infection rate. First, the thermally altered tissue is recognized as a foreign substance, which stimulates the immune system. Then, the immune system is overwhelmed as immune system cells become less effective and the production of the chemicals that normally provide resistance to infections decreases (see chapter 14). The greater the magnitude of the burn, the greater the depression of the immune system, and the greater the risk of infection.

TABLE 5.1 REPRESENTATIVE DISEASES AND DISORDERS: Skin

Condition	Description
Ringworm	Fungal infection that produces patchy scaling and inflammatory response in the skin
Eczema and dermatitis	Inflammatory conditions of the skin caused by allergy, infection, poor circulation, or exposure to chemical or environmental factors
Psoriasis	Chronic skin disease characterized by thicker than normal epidermal layer (stratum corneum) that sloughs to produce large, silvery scales; bleeding may occur if the scales are scraped away
Bacterial Infections	
Impetigo	Small blisters containing pus; easily rupture to form a thick, yellowish crust; usually affects children
Decubitus ulcers (bedsores or pressure sores)	Develop in people who are bedridden or confined to a wheelchair; compression of tissue and reduced circulation result in destruction of the subcutaneous tissue and skin, which later become infected by bacteria, forming ulcers
Viral Infections	
Rubeola (measles)	Skin lesions; caused by a virus contracted through the respiratory tract; may develop into pneumonia or infect the brain, causing damage
Rubella (German measles)	Skin lesions; usually mild viral disease contracted through the respiratory tract; may be dangerous if contracted during pregnancy because the virus can cross the placenta and damage the fetus
Chicken pox	Skin lesions; usually mild viral disease contracted through the respiratory tract
Shingles	Painful skin lesions that can recur when the dormant virus is activated by trauma, stress, or another illness; caused by the chicken pox virus after childhood infection
Cold sores (fever blisters)	Skin lesions; caused by herpes simplex I virus; transmitted by oral or respiratory routes; lesions recur
Genital herpes	Genital lesions; caused by herpes simplex II virus; transmitted by sexual contact

6. Critical Thinking Practice

The textbook presents you with multiple opportunities to practice applying the information you've learned to particular situations. Critical Thinking questions require a higher-order level of thinking than simple fact-based questions. The Bloom's Taxonomy icon indicates the level at which a given question is ranked.

a. Learn to Apply It

This feature appears at the beginning of each chapter and integrates information from earlier chapters or asks you to think about a scenario as you read the chapter. Answers to odd-numbered questions are provided online or in

the appendices. The answers are written in a solution-style format. We walk you through the logic of each answer.

LEARN TO APPLY IT

Rafael is playing the soccer match of his life. However, hot weather conditions are making this match one of his hardest yet. As the game began, Rafael noticed himself sweating, which was helping to keep him cool. However, he had been ill the night before and had not been able to hydrate as was normal for him. Toward the end of the second half, he realized he was no longer sweating and he began to feel overheated and dizzy.

Chapter 2

Learn to Apply It (Answer)

In this question, you learn that Rafael had not been able to properly hydrate the night before the soccer match and the weather is hot. The question also tells you that Rafael was cool when he was sweating and became overheated when he stopped sweating. Sweat consists mainly of water, and as you learned in section 2.1, water molecules are polar, allowing them to hydrogen-bond together. Later, in section 2.4, you learned that hydrogen bonds stabilize water, allowing it to absorb large amounts of heat. Thus, sweating.

b. Apply It

Apply It questions are distributed throughout each chapter and pertain to information presented prior to each question. The same solution-style format answers to the odd-numbered questions are provided.

Apply

Apply It 3

Provide the correct directional term for the following statement:
When a boy is standing on his head, his nose is _____ to his mouth.

c. Critical Thinking

Critical Thinking questions typically require a higher-order level of thinking than the Apply It questions. Solution-style-format answers are also provided for these.

CRITICAL THINKING

1. A male has lost blood as a result of a gunshot wound. Even though the bleeding has been stopped, his blood pressure is low and dropping, and his heart rate is elevated. Following a blood transfusion, his blood pressure increases and his heart rate decreases. Propose a physiological explanation for these changes.
2. During physical exercise, the respiration rate increases. Two students are discussing the mechanisms involved. Student A claims they are positive-feedback mechanisms, and student B claims they are negative-feedback mechanisms. Do you agree with student A or student B, and why?
3. Of the six characteristics of life, why is organismal reproduction a characteristic of life?
4. Describe, using as many directional terms as you can, the relationship between your kneecap and your heel.

7. Figure Colors and Symbols

Following are symbols used consistently to indicate the same structure or event in all chapters. If in some chapter a symbol is given a different usage, that usage for the symbol is always labeled or defined.

Symbol	**Meaning**
	Information and level flow
	Describe steps in a process
	To decrease or inhibit
	To increase or stimulate
	Channel proteins and ions Pink: Na^+ Purple: K^+ Green: Ca^{2+}
	Blue: Phospholipid bilayer of cell membrane Yellow: Cytoplasm/inside of cell
	Sodium/potassium pump

Acetylcholine

Sympathetic nervous system

Parasympathetic nervous system

Action potential

Generic ligand

Generic ligand receptor

G Protein

Veins with deoxygenated blood

Arteries with oxygenated blood

CONCLUSIONS

In our teaching we have seen, time and time again, that the students who put in the effort and utilize the activities described in this guide consistently outperform the students who do not. Thus, it will be your perseverance, sometimes called *grit*—and not how "smart" you are—that will enable your success. Encourage yourself, believe in yourself, and never quit.

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

1

The Human Organism

The human body is a complex system. The structures in the body work in concert to maintain homeostasis, a balance in the body's internal environment.

LEARN TO APPLY IT

Renzo, a dancer, can move his body such that it is perfectly balanced, yet a slight movement in any direction would cause him to adjust his position. The human body adjusts its balance among all its parts through a process called homeostasis.

Let's imagine that Renzo is suffering from a blood sugar disorder. Earlier, he'd eaten an energy bar. As an energy bar is digested, blood sugar rises. Normally, tiny collections of cells embedded in the pancreas respond to the rise in blood sugar by secreting the chemical insulin. Insulin increases the movement of sugar from the blood into the cells. However, Renzo did not feel satisfied from his energy bar. He felt dizzy and was still hungry, all symptoms he worried could be due to a family history of diabetes. Fortunately, the on-site trainer tested his blood sugar and noted that it was much higher than normal. After a visit to his regular physician, Renzo was outfitted with an insulin pump and his blood sugar levels are more consistent.

What is a good explanation for Renzo's blood sugar levels before and after his visit to the doctor?

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

1.1 ANATOMY AND PHYSIOLOGY

Learning Outcomes *After reading this section, you should be able to*

A. Define anatomy and describe the levels at which anatomy can be studied.
B. Explain the importance of the relationship between structure and function.
C. Define physiology and describe the levels at which physiology can be studied.

What lies ahead is a fantastic adventure—learning about the structure and function of the human body and the intricate checks and balances that regulate it. Perhaps you have had the experience of oversleeping, rushing to your 8 a.m. class, and missing breakfast. Afterward, on the way to your Anatomy & Physiology class, you bought an energy bar from the vending machine. Eating the energy bar helped you feel better. The explanation for this experience is the process of homeostasis, the maintenance of a relatively constant internal environment despite fluctuations in the external environment. For you, homeostasis was maintained, but for Renzo, the dancer in this chapter's Learn to Apply It feature, there was a disruption in homeostasis. Throughout this book, the major underlying theme is homeostasis. As you think about Renzo's case, you will come to realize just

how capable the human body is of an incredible coordination of thousands upon thousands of processes.

Learning about human anatomy and physiology is important for understanding disease. The study of human anatomy and physiology is important for students who plan a career in the health sciences because health professionals need a sound knowledge of structure and function in order to perform their duties. In addition, understanding anatomy and physiology prepares all of us to evaluate recommended treatments, critically review advertisements and reports in the popular literature, and rationally discuss the human body with health professionals and nonprofessionals.

Anatomy (ah-NAT-oh-mee) is the scientific discipline that investigates the structure of the body—for example, the parts and chambers of the heart. The word *anatomy* means to dissect, or cut apart and separate, the parts of the body for study. In addition, anatomy examines the relationship between the structure of a body part and its function. For example, the structure of a hammer informs us of its primary use of driving nails into wood. Similarly, the fact that bone tissue is a hard, mineralized substance enables the bones to provide strength and support. Understanding the relationship between structure and function makes it easier to understand and appreciate anatomy.

There are two basic approaches to the study of anatomy: (1) systemic anatomy and (2) regional anatomy. **Systemic anatomy** is the study of the body by systems, such as the cardiovascular, nervous, skeletal, and muscular systems. It is the approach taken in this textbook. **Regional anatomy** is the study of the organization of the body by areas. Within each region, such as the head, abdomen, or arm, all systems are studied simultaneously. This is the approach taken in many medical and dental schools.

Anatomists have two general ways to examine the internal structures of a living person: (1) surface anatomy and (2) anatomical imaging. **Surface anatomy** is the study of external features, such as bony projections, which serve as landmarks for locating deeper structures. For example, the sternum (breastbone) is used by health professionals as a landmark for listening to heart sounds. **Anatomical imaging** involves the use of x-rays, ultrasound, magnetic resonance imaging (MRI), and other technologies to create pictures of internal structures, such as when determining if a bone is broken or a ligament is torn. Both surface anatomy and anatomical imaging provide important information for diagnosing disease.

Physiology (fiz-ee-OL-oh-jee; the study of nature) is the scientific discipline that deals with the processes or functions of living things—it is important in physiology to recognize structures as dynamic. There are two major goals when studying physiology: (1) examining the body's responses to stimuli and (2) examining the body's maintenance of stable internal

conditions. **Human physiology** is the study of humans. Like anatomy, physiology can be studied at multiple levels. For example, **cellular physiology** focuses on processes inside cells such as the manufacturing of substances, including proteins, whereas **systemic physiology** focuses on the functions of organ systems.

1.2 STRUCTURAL AND FUNCTIONAL ORGANIZATION OF THE HUMAN BODY

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the six levels of organization of the body, and describe the major characteristics of each level.

B. List the eleven organ systems, identify their components, and describe the major functions of each system.

The body can be studied at six structural levels: chemical, cell, tissue, organ, organ system, and organism (figure 1.1).

PROCESS Figure

PROCESS Figure 1.1 **Levels of Organization for the Human Body**

The simplest level of organization in the human body is the atom. Atoms combine to form molecules. Molecules aggregate into cells. Cells form tissues, which combine with other tissues to form organs. Organs work in groups called organ systems. All organ systems work together to form an organism.

1.1(6) BJI/Blue Jean Images/Getty Images

Why is the skin considered an organ? What characterizes the integumentary system as an organ system?

1 Chemical Level

The structural and functional characteristics of all organisms are determined by their chemical makeup. The chemical level of organization involves how atoms, such as hydrogen and carbon, interact and combine into molecules.

This is important because a molecule's structure determines its function. For example, collagen molecules are strong, ropelike fibers that give skin structural strength and flexibility. With aging, the structure of collagen changes, and the skin becomes fragile and more easily torn during everyday activities. We present a brief overview of chemistry in chapter 2.

❷ Cell Level

Cells are the basic structural and functional units of organisms, such as plants and animals. Most cells contain smaller structures inside them, called **organelles** (OR-gah-nellz; little organs). Organelles carry out particular functions, such as digestion and movement, for the cell. For example, the nucleus contains the cell's hereditary information, and mitochondria manufacture adenosine triphosphate (ATP), a molecule cells use for a source of energy. Although cell types differ in their structure and function, they have many characteristics in common. Knowledge of these characteristics as well as their variations is essential to understanding anatomy and physiology. We discuss the cell in chapter 3.

MICROBES IN YOUR BODY

Getting to Know Your Bacteria

Did you know that you have more microbial cells than human cells in your body? Astoundingly, for every cell in your body, there is one microbial cell. That's as many as 40 trillion microbial cells, which collectively can account for 2 to 6 pounds of your body weight! A microbe is any life form that can only be seen with a microscope (for example, bacteria, fungi, and protozoa). All living organisms fit into one of three domains of living organisms: (1) Bacteria, (2) Archaea, and (3) Eukarya. The cells of organisms in each domain are unique. Bacterial cells' genetic material is not separated from the rest of the cell by a barrier. In addition, bacterial cells have far fewer separate structures made of membrane for carrying out the cell's metabolic processes than eukaryotic cells. Archaea cells are constructed similarly to bacteria; however, they share certain structures, called ribosomes, with eukaryotic cells. We will discuss cell structure in detail in chapter 3. Commonly, the term prokaryotic is used to describe bacterial and archaea cells. Eukarya cells, which include human cells, have the most structural complexity with many smaller structures, called organelles, surrounded by membranes. These smaller structures conduct the metabolic processes of the cell.

In addition to structural differences, there are many other differences far too numerous to adequately describe here. However, size differences between bacteria and archaea and cells of eukaryotes is quite evident with most eukaryotic cells being significantly larger than most prokaryotic cells. The total population of microbial cells on the human body is referred to as the microbiota, while the collection of all the microbial cell genes is known as the microbiome. The microbiota includes so-called good bacteria, which do not cause disease and may even help us. It also includes pathogenic, or "bad," bacteria.

With that many microbes in and on our bodies, you might wonder how they affect our health. To answer that question, the National Institutes of Health (NIH) initiated the Human Microbiome Project. Five significant regions of the human body were examined: the airway, skin, mouth, gastrointestinal tract, and vagina. This project identified over 5000 species and sequenced over 20 million unique microbial genes.

What did scientists learn from the Human Microbiome Project? Human health is dependent upon the health of our microbiota, especially the "good" bacteria. More specifically, the human microbiome is intimately involved in the development and maintenance of the immune system. And more evidence is mounting for a correlation between a host's microbiota, digestion, and metabolism. Researchers have suggested that microbial genes are more responsible for our survival than human genes are. There are even a few consistent pathogens that are present without causing disease, suggesting that their presence may be good for us. However, there does not seem to be a universal healthy human microbiome. Rather, the human microbiome varies across life span, ethnicity, nationality, culture, and geographic location. Instead of being a detriment, this variation may actually be very useful for predicting disease. There seems to be a correlation between autoimmune and inflammatory diseases (Crohn's disease, asthma, multiple sclerosis), which have become more prevalent, and a "characteristic microbiome community." Early research seems to indicate that any significant change in the profile of the microbiome of the human gut may increase a person's susceptibility to autoimmune diseases. It has been proposed that these changes may be associated with exposure to antibiotics, particularly in infancy. Fortunately, newer studies of microbial transplantations have shown that the protective and other functions of bacteria can be transferred from one person to the next. However, this work is all very new, and much research remains to be done.

Throughout this text, we will highlight specific instances in which our microbes influence our body systems. In light of the importance of our bodies' bacteria and other microbes, the prevalence of antibacterial soap and hand gel usage in everyday life may be something to think about.

❸ Tissue Level

A **tissue** (TISH-you) is a group of similar cells and the materials surrounding them. The characteristics of the cells and surrounding materials determine the functions of the tissue. The many tissues that make up the body are classified into four primary types: (1) epithelial, (2) connective, (3) muscle, and (4) nervous. We discuss tissues in chapter 4.

❹ Organ Level

An **organ** (OR-gan; a tool) is composed of two or more tissue types that together perform one or more common functions. For example, the heart,

stomach, liver, and urinary bladder are all organs (figure 1.2).

❺ Organ System Level

An **organ system** is a group of organs that together perform a common function or set of functions. For example, the urinary system consists of the kidneys, ureters, urinary bladder, and urethra. The kidneys produce urine, which is transported by the ureters to the urinary bladder, where it is stored until being eliminated from the body through the urethra. In this text, we consider eleven major organ systems: (1) integumentary, (2) skeletal, (3) muscular, (4) nervous, (5) endocrine, (6) cardiovascular, (7) lymphatic, (8) respiratory, (9) digestive, (10) urinary, and (11) reproductive. Figure 1.3 presents a brief summary of these organ systems and their functions.

Figure 1.2 **Major Organs of the Body**

The body's major organs include the brain, lungs, heart, liver, pancreas, spleen, stomach, gallbladder, kidneys, large intestine, small intestine, urinary bladder, and urethra.

Integumentary System

Provides protection, regulates temperature, prevents water loss, and helps produce vitamin D. Consists of skin, hair, nails, sebaceous glands, and sweat glands.

Skeletal System

Provides protection and support, allows body movements, produces blood cells, and stores minerals and adipose tissue. Consists of bones, associated cartilages, ligaments, and joints.

Muscular System

Produces body movements, maintains posture, and produces body heat. Consists of muscles attached to connective tissue sheets or the skeleton by tendons.

Nervous System

A major regulatory system that detects sensations and controls movements, physiological processes, and intellectual functions. Consists of the brain, spinal cord, nerves, and sensory receptors.

Endocrine System

A major regulatory system that influences metabolism, growth, reproduction, and many other functions. Consists of endocrine glands, including the hypothalamus, pituitary, thyroid gland, adrenal gland, gonads, and other tissues that secrete hormones.

Cardiovascular System

Transports nutrients, waste products, gases, and hormones throughout the body; plays a role in the immune response and the regulation of body temperature. Consists of the heart, blood vessels, and blood.

Figure 1.3 APR **Organ Systems of the Body**

There are 11 body systems: integumentary, skeletal, muscular, lymphatic, respiratory, digestive, nervous, endocrine, cardiovascular, urinary, and reproductive.

CLINICAL IMPACT

Cadavers and the Law

The study of human bodies is the foundation of medical education, and for much of history, anatomists have used the bodies of people who have died, called cadavers, for these studies. However, historically, public sentiment has made it difficult for anatomists to obtain human bodies for dissection. In the early 1800s, the benefits of human dissection for training physicians had become very apparent, and the need for cadavers increased beyond the ability to acquire them legally. Thus arose the resurrectionists, or body snatchers. For a fee and no questions asked, they removed bodies from graves and provided them to medical schools. Because the bodies were not easy to obtain and were not always in the best condition, two enterprising men named William Burke and William Hare went one step further. Over a period of time, they murdered seventeen people in Scotland and sold their bodies to a medical school. When discovered, Hare testified against Burke and went free. Burke was convicted, hanged, and publicly dissected. Discovery of Burke's activities so outraged the public that sensible laws regulating the acquisition of cadavers were soon passed, and this dark chapter in the history of anatomy was closed.

Today, in the United States, it is quite simple to donate your body for scientific study. The Uniform Anatomical Gift Act allows individuals to donate their organs or entire cadaver by putting a notation on their driver's license. You need only to contact a medical school or private agency to file the forms that give them the rights to your cadaver. Once the donor dies, the family of the deceased usually pays only the transportation costs for the remains. After dissection, the body is cremated, and the cremains can be returned to the family.

Throughout this text book, each Systems Pathology essay presents a specific disease state and considers how this affects the interactions of the organ systems.

6 Organism Level

An **organism** is any living thing considered as a whole, whether composed of one cell, such as a bacterium, or of trillions of cells, such as a human. The human organism is a network of organ systems that are mutually dependent upon one another.

1.3 CHARACTERISTICS OF LIFE

Learning Outcome *After reading this section, you should be able to*

A. List and define six characteristics of life.

Humans are organisms sharing characteristics with other organisms. The most important common feature of all organisms is life. This textbook recognizes six essential characteristics of life:

1. **Organization** refers to the specific interrelationships among the individual parts of an organism, and how those parts interact to perform specific functions. Living things are highly organized. All organisms are composed of one or more cells. In turn, cellular function depends on the precise organization of large molecules. Disruption of this organized state can result in loss of functions.
2. **Metabolism** (meh-TAB-oh-lizm) is the ability to use energy to perform other vital functions, such as growth, movement, and reproduction. Human cells possess specialized proteins that can break down food molecules to use as a source of energy.
3. **Responsiveness** is an organism's ability to sense changes in the external or internal environment and adjust to those changes. Responses include actions such as moving toward food or water and moving away from danger or poor environmental conditions such as extreme cold or heat. Organisms can also make adjustments that maintain their internal environment. For example, if our body temperature rises, sweat glands produce sweat, which can lower body temperature down to the normal range.
4. **Growth** refers to an increase in the size or number of cells, which produces an overall enlargement in all or part of an organism, cell size, or the amount of substance surrounding cells. For example, bones grow when the number of bone cells increases and the bone cells become surrounded by mineralized materials.
5. **Development** includes the changes an organism undergoes through time, beginning with fertilization and ending at death. Development usually involves growth, but it also involves differentiation. **Differentiation** involves changes in a cell's structure and function from an immature, generalized state to a mature, specialized state. For example, following fertilization, immature cells differentiate to become specific types of cells, such as skin, bone, muscle, or nerve cells. These differentiated cells form tissues and organs.
6. **Reproduction** is the formation of new cells or new organisms. Reproduction of cells allows for growth and development. Formation of new organisms prevents extinction of species.

1.4 HOMEOSTASIS

Learning Outcomes *After reading this section, you should be able to*

A. Define homeostasis, and explain why it is important for proper body function.
B. Describe a negative-feedback mechanism and give an example.
C. Describe a positive-feedback mechanism and give an example.

Homeostasis (hoh-mee-oh-STAY-sis; *homeo-,* the same; *-stasis*, to stop) is the maintenance of a relatively constant environment within the body. To achieve homeostasis, the body must actively regulate body conditions that are constantly changing. As our bodies undergo their everyday processes, we are continuously exposed to new conditions, both internally and externally. Changes in our environmental conditions, such as moving into hot or cold outdoor temperatures, can result in a change in our body temperature. Body temperature is one of our body's **variables**. These changes in body conditions are called variables because their values are not constant. For cells to function normally, the volume, temperature, and chemical content of the cells' environment must be maintained within a narrow range. Body temperature is a variable that increases when you are too hot and decreases when you are too cold.

The homeostatic mechanisms that maintain normal body temperature include sweating or shivering to maintain body temperature near an ideal normal value, or **set point** (figure 1.4). Most homeostatic mechanisms are regulated by the nervous system or the endocrine system. Note that homeostatic mechanisms are not able to maintain body temperature *precisely* at the set point. Instead, body temperature increases and decreases slightly around the set point, producing a **normal range** of values. As long as body temperatures remain within this normal range, homeostasis is maintained. Keep in mind that these fluctuations are minimal. Note in figure 1.4*a* that the normal body temperature range is no more than 1°F above or below normal. Our *average* body temperature is 98.6°F. Just as your home's thermostat does not keep the air temperature at exactly 75°F at all times, your body's temperature is not kept at exactly 98.6°F at all times.

PROCESS Figure

Body temperature (normal range)
98.8°F
98.6°F
98.4°F
Set point
(a)
Time (min)
Time (min)
1 Increased temperature
2 Control center (brain)
3 Increased sweating
4 Sweating stops
(b)
Uterine stretch stimulates sensory neurons
Control center
Uterus
Oxytocin
Uterine smooth muscles contract
Increased uterine stretch
Control center
Oxytocin
Increased contraction
1 Stretch of the uterus (receptors) signals the control center to increase contractions of the uterus (effector).
2 Continued stretch of the uterus signals the control center to further increase contractions.
Mammary

PROCESS Figure 1.4 **Negative- and Positive-Feedback Mechanisms**
(a) Homeostasis is the maintenance of a variable around an ideal normal value, or set point. The value of the variable fluctuates around the set point to establish a normal range of values. *(b)* Negative feedback is one of the mechanisms by which homeostasis is maintained. Receptors signal the control center, which regulates the action of the effectors. In the example, body temperature is too high, so sweating occurs. Negative feedback stops the sweating when the body temperature returns to normal. *(c)* Positive feedback is also a type of mechanism that works to maintain homeostasis. Receptors signal the control center that the cervix is being stretched, which results in the control center sending signals to increase the contractions of the uterus. This cycle continues, becoming stronger over time until the baby is born.

Occasionally an individual will not be able to produce sweat and can overheat, potentially suffering a heat stroke. Within the context of the body temperature homeostatic mechanism, where might the disruption occur? Propose at least three ways sweat production might be inhibited when the body temperature rises above the set point.

The organ systems help keep the body's internal environment relatively constant. For example, the digestive, respiratory, cardiovascular, and urinary systems function together so that each cell in the body receives adequate oxygen and nutrients while also ensuring that waste products do not accumulate to a toxic level. If body fluids deviate from homeostasis, body cells do not function normally and can even die. Disease disrupts homeostasis and sometimes results in death. Modern medicine attempts to understand disturbances in homeostasis and works to reestablish a normal range of values.

Negative Feedback

Most systems of the body are regulated by **negative-feedback mechanisms** which maintain homeostasis. In everyday terms, the word *negative* is used to mean "bad" or "undesirable." In this context, negative

means “to decrease.” *Negative feedback* is when any deviation from the set point is made smaller or is resisted. Negative feedback does not prevent variation but maintains variation within a normal range.

The maintenance of normal body temperature is an example of a negative-feedback mechanism. Normal body temperature is critical to our health because it allows molecules and enzymes to keep their normal shape so they can function optimally. An optimal body temperature prevents molecules from being permanently destroyed. Picture the change in appearance of egg whites as they are cooked: the egg whites change from a transparent liquid to a white solid because the heat changes the shape of the egg white molecules. Similarly, if the body is exposed to extreme heat, the shape of the molecules in the body could change, which would eventually prevent them from functioning normally.

Most negative-feedback mechanisms have three components: (1) A **receptor** (ree-SEP-tor), which monitors the value of a variable, such as body temperature, by detecting stimuli; (2) a **control center,** such as part of the brain, which determines the set point for the variable and receives input from the receptor about the variable; and (3) an **effector** (ee-FEK-ter), such as the sweat glands, which can adjust the value of the variable when directed by the control center, usually back toward the set point. A changed variable is a **stimulus** because it initiates a homeostatic mechanism. Several negative-feedback mechanisms regulate body temperature, and they are described more fully in chapter 5.

Figure 1.4*b* demonstrates the steps in the negative-feedback regulation of body temperature if it becomes too high. Normal body temperature depends on the coordination of multiple structures, which are regulated by the control center (the hypothalamus).

❶ Receptors in the skin monitor body temperature. If body temperature rises, the receptors send a message to the control center.

❷ The control center compares the value of the variable against the set point.

❸ If a response is necessary, the control center will stimulate the effectors, the sweat glands, to produce their response, which is secretion of sweat.

❹ Once the value of the variable has returned to the set point, the effectors do not receive any more information from the control center. For body temperature, this means that secretion of sweat stops. These same steps can be used to help you answer the Learn to Apply It question at the beginning of this chapter.

Often there is more than one effector for a particular homeostatic mechanism. In these cases the control center must coordinate the effectors' responses. For example, cooling the body involves not only the production of sweat by the sweat glands, but also the action of the blood vessels to alter blood flow to the skin. Once body temperature has returned to normal, the effectors stop. This is the hallmark of negative feedback—effectors stop their response once the variable has returned to its set point. They do not produce an indefinite response (figure 1.5).

Homeostasis Figure 1.5 **Negative-Feedback Control of Body Temperature**

Throughout this book, all homeostasis figures have the same format as shown here. The changes caused by the increase of a variable outside the normal range are shown in the upper, *green boxes,* and the changes caused by a decrease are shown in the lower, *red boxes*. To help you learn how to interpret homeostasis figures, some of the steps in this figure are numbered. (1) Body temperature is within its normal range. (2) Body temperature increases outside the normal range, which causes homeostasis to be disturbed. (3) The body temperature control center in the brain responds to the change in body temperature. (4) The control center causes sweat glands to produce sweat and blood vessels in the skin to dilate. (5) These changes cause body temperature to decrease. (6) Body temperature returns to its normal range, and homeostasis is restored. Observe the responses to a decrease in body temperature outside its normal range by following the lower, *red arrows*.

Understand

Apply It 1

What effect would swimming in cool water have on body temperature regulation mechanisms? What would happen if a negative-feedback mechanism did not return the value of a variable, such as body temperature, to its normal range?

Positive Feedback

Positive-feedback mechanisms occur when a response to the original stimulus results in the deviation from the set point becoming even greater. In other words, *positive* means "increase." At times, this type of response is required to return to homeostasis. For example, during blood loss, a chemical responsible for blood clot formation, called thrombin, stimulates production of even more thrombin. In this way, a disruption in homeostasis is resolved through a positive-feedback mechanism. What prevents the entire vascular system from clotting? The clot formation process is self-limiting. Eventually, the components needed to form a clot will be depleted in the damaged area and more clot material cannot be formed.

As shown in figure 1.4c, birth is another example of a normally occurring positive-feedback mechanism.

❶ Near the end of pregnancy, the baby's large size stretches the uterus.

❷ This stretching, especially around the opening of the uterus, stimulates contractions of the uterine muscles.

❸ The uterine contractions push the baby against the opening of the uterus, which results in additional stretching.

❹ This positive-feedback sequence ends when the baby is delivered from the uterus and the stretching stimulus is eliminated.

Two basic principles about homeostatic mechanisms to remember are that (1) many disease states result from the failure of negative-feedback mechanisms to maintain homeostasis, and (2) some positive-feedback mechanisms can be detrimental instead of helpful. One example of a detrimental positive-feedback mechanism is inadequate delivery of blood to cardiac (heart) muscle. Contraction of cardiac muscle generates blood pressure. The heart pumps blood to itself through a system of blood vessels on the outside of the heart. Just as with other tissues, blood pressure must be maintained to ensure adequate delivery of blood to the cardiac muscle. Following extreme blood loss, such as a severe cut on the body, not enough

blood is delivered to cardiac muscle. As a result, the heart cannot function normally. The heart pumps less blood, which causes the blood pressure to drop even further, which causes even less blood to be delivered to the heart. The process continues until the heart stops beating, and death results. In this example, we see the deviation from the heart-rate set point becoming larger and larger—this is the hallmark of positive feedback. Thus, if blood loss is severe, negative-feedback mechanisms may not be able to maintain homeostasis and the positive feedback of ever-decreasing blood pressure can develop.

On the other hand, following a moderate amount of blood loss (e.g., after donating a pint of blood), *negative-feedback mechanisms* result in an *increase* in heart rate that restores blood pressure.

Apply It 2

Is the sensation of thirst associated with a negative- or a positive-feedback mechanism? Explain. (Hint: What is being regulated when you become thirsty?)

1.5 TERMINOLOGY AND THE BODY PLAN

Learning Outcomes ***After reading this section, you should be able to***

A. Describe a person in anatomical position.
B. Define the directional terms for the human body, and use them to locate specific body structures.
C. Know the terms for the parts and regions of the body.
D. Name and describe the three major planes of the body and the body organs.
E. Name and describe the three major ways to cut an organ.
F. Describe the major trunk cavities and their divisions.
G. Describe the serous membranes, their locations, and their functions.

As you study anatomy and physiology, you will be learning many new words. Knowing the **etymology** (ET-ee-MOL-oh-jee) of these words can make learning them easy and fun. Most anatomical terms are derived from Latin or Greek. For example, *foramen* is a Latin word for "hole," and *magnum* means "large." The foramen magnum is therefore a large hole in the skull (through which the spinal cord continues from the brain).

Words are often modified by adding a prefix or suffix. For example, the suffix *-itis* means an inflammation, so *appendicitis* is an inflammation of the appendix. As new terms are introduced in this text, their meanings are often

explained. The glossary and the list of word roots, prefixes, and suffixes also provide additional information about the new terms.

Body Positions

Anatomical position refers to a person standing upright with the face directed forward, the upper limbs hanging to the sides, and the palms of the hands facing forward (figure 1.6). A person is **supine** when lying face upward and **prone** when lying face downward.

Figure 1.6 APR **Directional Terms**

All directional terms are in relation to the body in the anatomical position: a person standing erect with the face directed forward, the arms hanging to the sides, and the palms of the hands facing forward.

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In anatomical position, the head is above the feet, but if a person were to do a handstand, the head would be closer to the ground than the feet were. However, we would still refer to the head as being "above" the feet because the point of reference for anatomical structures is their position on the body, not the position of the body compared to the earth.

Directional Terms

Directional terms describe parts of the body relative to each other (figure 1.6 and table 1.1). It is important to become familiar with these directional terms as soon as possible because you will see them repeatedly throughout the text. *Right* and *left* are used as directional terms in anatomical terminology. In anatomy, the term **superior** means *above,* and the term **inferior** means *below*. **Anterior** is used for "in front of" and the term **posterior** is used for "behind."

TABLE 1.1 Directional Terms for the Human Body

Term	Etymology	Definition*	Example
Right		Toward the body's right side	The right ear
Left		Toward the body's left side	The left ear
Inferior	Lower	Below	The nose is inferior to the forehead.
Superior	Higher	Above	The mouth is superior to the chin.
Anterior	To go before	Toward the front of the body	The teeth are anterior to the throat.
Posterior	*Posterus*, following	Toward the back of the body	The brain is posterior to the eyes.
Dorsal	*Dorsum*, back	Toward the back (synonymous with *posterior*)	The spine is dorsal to the breastbone.
Ventral	*Venter*, belly	Toward the belly (synonymous with *anterior*)	The navel is ventral to the spine.
Proximal	*Proximus*, nearest	Closer to a point of attachment	The shoulder is proximal to the elbow.
Distal	*di* + *sto*, to be distant	Farther from a point of attachment	The ankle is distal to the hip.
Lateral	*Latus*, side	Away from the midline of the body	The nipple is lateral to the breastbone.
Medial	*Medialis*, middle	Toward the middle or midline of the body	The bridge of the nose is medial to the eye.
Superficial	*Superficialis*, surface	Toward or on the surface	The skin is superficial to muscle.
Deep	*Deop*, deep	Away from the surface, internal	The lungs are deep to the ribs.

Term	Etymology	Definition*	Example
*All directional terms refer to a human in the anatomical position.			

In human anatomy, two terms can be used interchangeably to refer to the front of the body (or an organ)—**anterior** and **ventral** (belly). Likewise, two terms can be used interchangeably to refer to the back of the body (or an organ)—**posterior** and **dorsal** (back).

Proximal means "close to," whereas **distal** means "far from." These terms are used to refer to relative positions of structures, such as on the limbs. Each limb is attached at its proximal end to the body, and the distal end, such as the hand, is farther away. "Proximal" and "distal" can also describe one structure's position relative to another's, such as specialized structures in the kidney called the proximal and distal convoluted tubules. Their position is described relative to another kidney structure.

Medial means "toward the midline," and **lateral** means "away from the midline." The nose is located in a medial position on the face, and the ears are lateral to the nose. The term **superficial** refers to a structure close to the surface of the body, and **deep** is toward the interior of the body. For example, the skin is superficial to muscle and bone.

Apply It 3

Provide the correct directional term for the following statement: When a boy is standing on his head, his nose is _____ to his mouth.

Body Parts and Regions

Health professionals use a number of terms when referring to different regions or parts of the body. Figure 1.7 (*a,* anterior, and *b,* posterior) shows the anatomical terms, with the common terms in parentheses.

Figure 1.7 APR **Body Parts and Regions**

The anatomical and common (*in parentheses*) names are indicated for some parts and regions of the body. (*a*) Anterior view. (*b*) Posterior view.

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The central region of the body consists of the **head, neck,** and **trunk.** The trunk can be divided into three regions: (1) the **thorax**, (2) the **abdomen**, and (3) the **pelvis**. The thorax is the chest cavity where the heart and lungs are located. The abdomen contains organs such as (1) the liver, (2) the stomach, and (3) the intestines. The pelvis contains the bladder and reproductive organs. The upper limb is divided into (1) the arm, (2) the forearm, (3) the wrist, and (4) the hand. The **arm** extends from the shoulder to the elbow, and the **forearm** extends from the elbow to the wrist. The lower limb is divided into (1) the thigh, (2) the leg, (3) the ankle, and (4) the foot. The **thigh** extends from the hip to the knee, and the **leg** extends from the knee to the ankle. Note that, contrary to popular usage, the terms *arm* and *leg* refer to only a part of the limb.

The abdomen is often subdivided superficially into four **quadrants,** by two imaginary lines—one horizontal and one vertical—that intersect at the navel (figure 1.8*a*). The quadrants formed are (1) the right-upper, (2) the left-upper, (3) the right-lower, and (4) the left-lower quadrants. In addition to these quadrants, the abdomen is sometimes subdivided into **regions** by four imaginary lines—two horizontal and two vertical. These four lines create a "virtual" tic-tac-toe grid on the abdomen, resulting in nine regions: (1) epigastric (ep-ee-GAS-trik), (2, 3) right and left hypochondriac (high-poh-KON-dree-ack), (4) umbilical (um-BIL-ih-kal), (5, 6) right and left lumbar (LUM-bar), (7) hypogastric (high-poh-GAS-trik), and (8, 9) right and left iliac (IL-ee-ack) (figure 1.8*b*). Health professionals use the quadrants or regions as reference points for locating the underlying organs. For example, the appendix is in the right-lower quadrant, and the pain of an acute appendicitis is usually felt there.

Figure 1.8 **Subdivisions of the Abdomen**

Lines are superimposed over internal organs to demonstrate the relationship of the organs to the subdivisions. (*a*) Abdominal quadrants consist of four subdivisions. (*b*) Abdominal regions consist of nine subdivisions.

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Understand

Apply It 4

Using figures 1.2 and 1.8a, determine in which quadrant each of the following organs is located: spleen, gallbladder, kidneys, most of the stomach, and most of the liver.

Planes

At times it is useful to describe the body as having imaginary flat surfaces, called planes, passing through it (figure 1.9). A plane divides, or sections, the body, making it possible to "look inside" and observe the body's structures.

Figure 1.9 APR **Planes of Section of the Body**

(*a*) Planes of section through the body are indicated by "glass" sheets. Also shown are actual sections through (*b*) the head (*viewed from the right*), (*c*) the abdomen (*inferior view; liver is on the right*), and (*d*) the hip (*anterior view*).

(a) ©Eric Wise; (b,c,d) ©R. T. Hutchings

1. A **sagittal** (SAJ-ih-tal) **plane** separates the body or a structure into right and left halves. The word *sagittal* means "the flight of an arrow" and refers to the way the body would be split by an arrow passing anteriorly to posteriorly.
2. A **median plane** is a sagittal plane that passes through the midline of the body, dividing it into equal right and left halves.
3. A **transverse** (**horizontal**) **plane** runs parallel to the ground, dividing the body into superior and inferior portions.
4. A **frontal** (**coronal**) (KOR-oh-nal; crown) **plane** divides the body into front (anterior) and back (posterior) halves. For example, the coronal suture on the skull is located across the top, where a person might wear a crown.

Organs are often sectioned to reveal their internal structure (figure 1.10). A **longitudinal section** is a cut along the length of the organ, similar to the cut along a hot dog bun. A **transverse section,** or *cross section*, cuts completely through an organ, similar to cutting a hot dog or banana into round pieces. If a cut is made diagonally across the long axis, it is called an **oblique section.**

Figure 1.10 **Planes of Section Through an Organ**

Planes of section through the small intestine are indicated by "glass" sheets. The views of the small intestine after sectioning are also shown. Although the small intestine is basically a tube, the sections appear quite different in

shape.

Body Cavities

The body contains two types of internal cavities: (1) the dorsal body cavity and (2) the ventral body cavity (figure 1.11). These cavities, which are closed to the outside, contain our internal organs, providing protection for them. Some anatomy texts do not use the dorsal body cavity designation; however, in this textbook we have chosen to use the two internal body cavities model.

Figure 1.11 APR **Trunk Cavities**

(*a*) Anterior view showing the major trunk cavities. The diaphragm separates the thoracic cavity from the abdominal cavity. The mediastinum, which includes the heart, is a partition of organs dividing the thoracic cavity. (*b*) Sagittal section of the trunk cavities viewed from the left. The *dashed line* shows the division between the abdominal and pelvic cavities. The mediastinum has been removed to show the thoracic cavity.

Dorsal Body Cavity

The dorsal body encloses the organs of the nervous system, the brain and spinal cord. The two subdivisions of the dorsal body cavity are (1) the cranial cavity, which houses the brain, and (2) the vertebral canal, which houses the spinal cord. Both the brain and spinal cord are covered by membranes called

meninges (figure 1.11*a*). We discuss the anatomy of the nervous system further in chapters 12 and 13.

Ventral Body Cavity

The ventral body cavity houses the vast majority of our internal organs, collectively referred to as the **viscera** (VIS-er-ah; internal organs) (figure 1.11*b* and *c*). The ventral body cavity also has two major subdivisions, which are (1) the thoracic cavity and (2) the abdominopelvic cavity.

The Thoracic Cavity

The **thoracic cavity** is more superior to the abdominopelvic cavity and houses primarily the heart and lungs, among other organs. This cavity is further subdivided into sections: (1) two lateral **pleural cavities,** each of which encloses a lung, and are surrounded by the ribs, and (2) a medial **mediastinum** (MEE-dee-ah-STIE-num; middle wall), which houses the heart and its major blood vessels, in addition to the thymus, the trachea, and the esophagus.

The Abdominopelvic Cavity

The **abdominopelvic cavity** is enclosed by abdominal muscles and consists of (1) the more superior **abdominal cavity** and (2) the more inferior **pelvic cavity.** The organs of the abdominopelvic cavity are housed within the **peritoneal** (per-ih-toh-NEE-al; to stretch over) **cavity.** The abdominal cavity contains the majority of the digestive organs, such as the stomach, the intestines, and the liver, in addition to the spleen. The pelvic cavity continues below the pelvis and contains the urinary bladder, urethra, rectum of the large intestine, and reproductive organs.

Serous Membranes of the Ventral Body Cavity

The walls of the body cavities and the surface of internal organs are in contact with membranes called **serous** (SEER-us) **membranes.** These membranes are double layered. The layer that lines the walls of the cavities is called the **parietal** (pah-RYE-eh-tal; wall) **serous membrane.** The layer covering the internal organs (the viscera) is the **visceral serous membrane.** To understand the relationship between the parietal and the visceral serous membranes, imagine pushing your fist (representing an organ) into a slightly deflated balloon (representing the membranes and the cavity) (figure 1.12). Since your fist represents the internal organs, the portion of the balloon in contact with your fist represents the visceral serous membrane, and the outer part of the balloon wall represents the parietal serous membrane. However, in

the body, the parietal serous membrane is in close contact with the body cavity wall. Furthermore, in the body, there is no air between the visceral and parietal serous membranes as there is in the balloon; rather, the two membranes are separated by a thin film of serous fluid produced by the membranes. As organs move around in the cavities, the combination of serous fluid and smooth serous membranes reduces friction.

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Figure 1.12 **Serous Membranes**

(*a*) Fist pushing into a balloon. A "glass" sheet indicates the location of a cross section through the balloon. (*b*) Interior view produced by the section in (*a*). The fist represents an organ, and the walls of the balloon represent the serous membranes. The inner wall of the balloon represents a visceral serous membrane in contact with the fist (organ). The outer wall of the balloon represents a parietal serous membrane. (*c*) View of the serous membranes surrounding the lungs. The membrane in contact with the lungs is the visceral pleura; the membrane lining the wall of the lung cavity is the parietal pleura.

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Thoracic Cavity Membranes

The serous membranes are named for the specific cavity and organs they are in contact with. They include:

1. **Pericardial Cavity.** The pericardial cavity (peri-, around; cardi-, heart), containing the heart, is housed in the mediastinum. The parietal serous membrane is called the **parietal pericardium** and the visceral serous membrane is called the **visceral pericardium.** The space between the two pericardial membranes is called the **pericardial cavity** and is filled with **pericardial fluid** (figure 1.13*a*).
2. **Pleural Cavities.** Each of the two pleural cavities (pleuron-, side of body, rib) houses a lung. The parietal serous membrane lining the pleural cavities is called

the **parietal pleura,** while the visceral serous membrane covering the lungs is called the **visceral pleura** (figure 1.13*b*). The space between the two pleural membranes is called the **pleural cavity** and is filled with **pleural fluid.**

3. **Peritoneal Cavity.** The peritoneal cavity (peri-, around; -tonos-, stretched; stretched around) houses many internal organs, such as the liver, the digestive organs, and the reproductive organs. The parietal serous membrane in the peritoneal cavity is called the **parietal peritoneum.** The visceral serous membrane is called the **visceral peritoneum.** The space between the two serous membranes is the specific location of the **peritoneal cavity** and is filled with **peritoneal fluid** (figure 1.13*c*). In addition to covering organs, a double-folded sheet of visceral peritoneum attaches the digestive organs at certain points to the posterior abdominopelvic cavity wall. These regions of double-folded visceral peritoneum are called **mesenteries.** The mesenteries also provide a pathway for nerves and blood vessels to reach the digestive organs (figure 1.13*d*). The most notable mesenteric structure is an enormous pouch containing adipose tissue that is suspended from the inferior border of the stomach. In some people, this pouch contributes to their "big belly" (see chapter 24).

Figure 1.13 **Location of Serous Membranes**

(*a*) Frontal section showing the parietal pericardium (*blue*), visceral pericardium (*red*), and pericardial cavity. (*b*) Frontal section showing the parietal pleura (*blue*), visceral pleura (*red*), and pleural cavities. (*c*) Sagittal section through the abdominopelvic cavity showing the parietal peritoneum (*blue*), visceral peritoneum (*red*), peritoneal cavity, mesenteries (*purple*), and retroperitoneal organs. (*d*) Photo of mesentery (*green*) in a cadaver.

(d) MCOF Enterprises, Ltd./McGraw Hill Education

Some abdominal organs are tightly adhered to the posterior body wall and are covered by peritoneum only on their peritoneal cavity side. These organs have a **retroperitoneal** (RE-troh-PER-i-toh-NEE-uhl; behind the peritoneum) location and include the kidneys, ureters, adrenal glands, a large portion of the pancreas, parts of the large intestine, and the urinary bladder (see figure 1.13).

Inflammation, often due to an infection, of the serous membranes in the ventral body cavities sometimes occurs. Serious consequences can arise if the inherent infection or problem cannot be resolved. The following is a list of the conditions caused by inflammation of the serous membranes:

1. **Pericarditis** (PER-i-kar-DIE-tis; *-itis*, inflammation) is inflammation of the pericardium.
2. **Pleurisy** (PLOOR-ih-see) is inflammation of the pleura.
3. **Peritonitis** (PER-ih-toe-NIGH-tis) is inflammation of the peritoneum.

Understand

Apply It 5

Explain how an organ can be located within the abdominopelvic cavity but not be within the peritoneal cavity.

SUMMARY

Knowledge of anatomy and physiology can be used to predict the body's responses to stimuli when healthy or diseased.

1.1 Anatomy and Physiology

1. Anatomy is the study of the structures of the body.

2. Systemic anatomy is the study of the body by organ systems. Regional anatomy is the study of the body by areas.
3. Surface anatomy uses superficial structures to locate deeper structures, and anatomical imaging is a noninvasive method for examining deep structures.
4. Physiology is the study of the processes and functions of the body.

1.2 Structural and Functional Organization of the Human Body

1. The human body can be organized into six levels: chemical, cell, tissue, organ, organ system, and organism.
2. The eleven organ systems are the integumentary, skeletal, muscular, nervous, endocrine, cardiovascular, lymphatic, respiratory, digestive, urinary, and reproductive systems (see figure 1.3).

1.3 Characteristics of Life

The characteristics of life are organization, metabolism, responsiveness, growth, development, and reproduction.

1.4 Homeostasis

Homeostasis is the condition in which body functions, body fluids, and other factors of the internal environment are maintained within a range of values suitable to support life.

Negative Feedback

Negative-feedback mechanisms maintain homeostasis.

Positive Feedback

Positive-feedback mechanisms make deviations from normal even greater. Although a few positive-feedback mechanisms normally exist in the body, most positive-feedback mechanisms are harmful.

1.5 Terminology and the Body Plan

Body Positions

1. A human standing erect with the face directed forward, the arms hanging to the sides, and the palms facing forward is in the anatomical position.
2. A face-upward position is supine and a face-downward one is prone.

Directional Terms

Directional terms always refer to the anatomical position, regardless of the body's actual position (see table 1.1).

Body Parts and Regions

1. The body can be divided into the head, neck, trunk, upper limbs, and lower limbs.
2. The abdomen can be divided superficially into four quadrants or nine regions, which are useful for locating internal organs or describing the location of a pain.

Planes

1. A sagittal plane divides the body into left and right parts, a transverse plane divides the body into superior and inferior parts, and a frontal plane divides the body into anterior and posterior parts.
2. A longitudinal section divides an organ along its long axis, a transverse section cuts an organ at a right angle to the long axis, and an oblique section cuts across the long axis at an angle other than a right angle.

Body Cavities

1. There are two internal body cavities: the dorsal body cavity and the ventral body cavity.
2. The dorsal body cavity houses the brain and the spinal cord.
3. The mediastinum subdivides the thoracic cavity.
4. The diaphragm separates the thoracic and abdominal cavities.

5. Pelvic bones surround the pelvic cavity.
6. Serous membranes line the trunk cavities. The parietal portion of a serous membrane lines the wall of the cavity, and the visceral portion is in contact with the internal organs.
   - The serous membranes secrete fluid, which fills the space between the visceral and parietal membranes. The serous membranes protect organs from friction.
   - The pericardial cavity surrounds the heart, the pleural cavities surround the lungs, and the peritoneal cavity surrounds certain abdominal and pelvic organs.

7. Mesenteries are parts of the peritoneum that hold the abdominal organs in place and provide a passageway for blood vessels and nerves to the organs.
8. Retroperitoneal organs are located “behind” the parietal peritoneum.

REMEMBERING AND UNDERSTANDING

1. Define anatomy, surface anatomy, anatomical imaging, and physiology.
2. List six structural levels at which the body can be studied.
3. Define tissue. What are the four primary tissue types?
4. Define organ and organ system. What are the eleven organ systems of the body and their functions?
5. Name six characteristics of life.
6. What does the term *homeostasis* mean? If a deviation from homeostasis occurs, what kind of mechanism restores homeostasis?
7. Describe a negative-feedback mechanism in terms of receptor, control center, and effector. Give an example of a negative-feedback mechanism in the body.
8. Define positive feedback. Why are positive-feedback mechanisms generally harmful? Give one example each of a harmful and a beneficial positive-feedback mechanism in the body.
9. Why is knowledge of the etymology of anatomical and physiological terms useful?
10. Describe the anatomical position. Why is it important to remember the anatomical position when using directional terms?
11. Define and give an example of the following directional terms: *inferior, superior, anterior, posterior, dorsal, ventral, proximal, distal, lateral, medial, superficial,* and *deep*.
12. List the subdivisions of the trunk, the upper limbs, and the lower limbs.

13. Describe the four-quadrant and nine-region methods of subdividing the abdomen. What is the purpose of these methods?
14. Define the sagittal, median, transverse, and frontal planes of the body.
15. Define the longitudinal, transverse, and oblique sections of an organ.
16. Define the following cavities: thoracic, abdominal, pelvic, and abdominopelvic. What is the mediastinum?
17. What is the difference between the visceral and parietal layers of a serous membrane? What function do serous membranes perform?
18. Name the serous membranes associated with the heart, lungs, and abdominopelvic organs.
19. Define mesentery. What does the term *retroperitoneal* mean? Give an example of a retroperitoneal organ.

CRITICAL THINKING

1. A male has lost blood as a result of a gunshot wound. Even though the bleeding has been stopped, his blood pressure is low and dropping, and his heart rate is elevated. Following a blood transfusion, his blood pressure increases and his heart rate decreases. Propose a physiological explanation for these changes.
2. During physical exercise, the respiration rate increases. Two students are discussing the mechanisms involved. Student A claims they are positive-feedback mechanisms, and student B claims they are negative-feedback mechanisms. Do you agree with student A or student B, and why?
3. Of the six characteristics of life, why is organismal reproduction a characteristic of life?
4. Describe, using as many directional terms as you can, the relationship between your kneecap and your heel.
5. In some traditions, a wedding band is worn closest to the heart, and an engagement ring is worn as a “guard” on the outside. Should a person’s wedding band be worn proximal or distal to the engagement ring?
6. In which quadrant and region would a person experience discomfort in the event of a urinary bladder infection?

7. During pregnancy, which would increase more in size, the mother's abdominal cavity or her pelvic cavity? Explain.
8. A bullet enters the left side of a male, passes through the left lung, and lodges in the heart. Name in order the serous membranes and the cavities through which the bullet passes.
9. Can a kidney be removed without cutting through the parietal peritoneum? Explain.

Answers to odd-numbered questions from this chapter appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

2

The Chemical Basis of Life

To thoroughly understand the structure and function of the human body, it helps to begin with the materials that compose our bodies and how those materials interact.

LEARN TO APPLY IT

Rafael is playing the soccer match of his life. However, hot weather conditions are making this match one of his hardest yet. As the game began, Rafael noticed himself sweating, which was helping to keep him cool. However, he had been ill the night before and had not been able to hydrate as was normal for him. Toward the end of the second half, he realized he was no longer sweating and he began to feel overheated and dizzy.

Explain how Rafael's inability to sweat affects his internal temperature.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 2 Cells and Chemistry

2.1 BASIC CHEMISTRY

Learning Outcomes *After reading this section, you should be able to*

A. Define chemistry.
B. State the relevance of chemistry to anatomy and physiology.
C. Define matter, mass, and weight.
D. Distinguish between an element and an atom.
E. Define atomic number and mass number.
F. Name the subatomic particles of an atom, and indicate their charge and their location in an atom.
G. Define electronegativity. Compare and contrast ionic and covalent bonds.
H. Explain how electronegativity determines the type of bond two atoms will form.
I. Explain what creates a hydrogen bond and relate its importance.
J. Differentiate between a molecule and a compound.
K. Describe the process of dissociation.

Chemicals make up the body's structures, and the interactions of chemicals with one another are responsible for the body's functions. The processes of nerve impulse generation, digestion, muscle contraction, and metabolism can all be described in chemical terms. Many abnormal conditions and their treatments can also be explained in chemical terms. For example, Parkinson disease, which causes uncontrolled shaking movements, results from a shortage of a chemical called dopamine in certain nerve cells in the brain. It can be treated by giving patients another chemical, which brain cells convert to dopamine.

To understand anatomy and physiology, it is essential to have a basic knowledge of chemistry—the scientific discipline concerned with the atomic composition of substances and the reactions they undergo. This chapter is not a comprehensive treatment of chemistry, but it does review some of the basic chemical concepts related to living systems. Refer back to this chapter when chemical processes are discussed later in the book.

Matter, Mass, and Weight

All living and nonliving things are composed of **matter,** which is anything that occupies space and has mass. **Mass** is the amount of matter in an object, and **weight** is the gravitational force acting on an object of a given mass. For example, the weight of an apple results from the force of gravity "pulling" on the apple's mass.

Apply It 1

The difference between mass and weight can be illustrated by considering an astronaut. How would an astronaut's mass and weight in outer space compare with that astronaut's mass and weight on the earth's surface?

The international unit for mass is the **kilogram (kg),** which is the mass of a platinum-iridium cylinder kept at the International Bureau of Weights and Measurements in France. The mass of all other objects is compared with this cylinder. For example, a 2.2-lb lead weight and 1 liter (L) (1.06 qt) of water each have a mass of approximately 1 kg. An object with 1/1000 the mass of the standard kilogram cylinder is said to have a mass of 1 **gram (g).**

Elements and Atoms

An **element** is the simplest type of matter having unique chemical properties. A list of the elements commonly found in the human body appears in table 2.1. About 96% of the body's weight results from the elements oxygen, carbon, hydrogen, and nitrogen. However, many other elements also play important roles in the human body. For example, calcium helps form bones, and sodium ions are essential for neuronal activity. Some of these elements are present in only trace amounts but are still essential for life.

Table 2.1 Common Elements in the Human Body

Element	Symbol	Atomic Number	Mass Number	Atomic Mass	Percent by Weight	Percent by Number of Atoms
Hydrogen	H	1	1	1.008	9.5	63.0
Carbon	C	6	12	12.01	18.5	9.5
Nitrogen	N	7	14	14.01	3.3	1.4
Oxygen	O	8	16	16.00	65.0	25.5
Fluorine	F	9	19	19.00	Trace	Trace
Sodium	Na	11	23	22.99	0.2	0.3
Magnesium	Mg	12	24	24.31	0.1	0.1
Phosphorus	P	15	31	30.97	1.0	0.22
Sulfur	S	16	32	32.07	0.3	0.05
Chlorine	Cl	17	35	35.45	.02	0.03
Potassium	K	19	39	39.10	0.4	0.06
Calcium	Ca	20	40	40.08	1.5	0.31
Iron	Fe	26	56	55.85	Trace	Trace
Iodine	I	53	127	126.9	Trace	Trace

An **atom** (AT-om; indivisible) is the smallest particle of an element that has the chemical characteristics of that element. An element is composed of atoms of only one kind. For example, the element carbon is composed of only carbon atoms, and the element oxygen is composed of only oxygen atoms.

An element, or an atom of that element, is often represented by a symbol. Usually the symbol is the first letter or letters of the element's name—for example, C for carbon, H for hydrogen, and Ca for calcium. Occasionally, the symbol is taken from the Latin, Greek, or Arabic name for the element; for example, the symbol for sodium is Na, from the Latin word *natrium*.

Atomic Structure

The characteristics of matter result from the structure, organization, and behavior of atoms. Atoms are composed of subatomic particles, some of which have an electrical charge. Like mass and weight, electrical charge is one of the fundamental properties of matter. Electrical charge is the tendency of particles to be attracted to each other or repulsed from each other. There are two types of electrical charge: positive and negative. Particles with opposite charge are attracted to each other while particles with the same charge are repulsed from each other. The three major types of subatomic particles are (1) neutrons, (2) protons, and (3) electrons. A **neutron** (NOO-tron) has no electrical charge, a **proton** (PROH-ton) has one positive charge, and an **electron** (ih-LEK-tron) has one negative charge. Since each atom has an equal number of protons and electrons, the positive and negative charges cancel each other. Therefore, each atom is electrically neutral.

Protons and neutrons are found in the center of the atom, which is called the **nucleus** (nucleus-, kernel, inner part). The electrons are found in an **electron cloud** and are constantly orbiting the nucleus (figure 2.1). The nucleus accounts for 99.97% of an atom's mass, but only 1-ten-trillionth of its volume. Most of the volume of an atom is occupied by the electrons, although it is impossible to know precisely where any given electron is located at any particular moment (figure 2.1).

Figure 2.1 **Hydrogen, Carbon, and Oxygen Atoms**

(*a*) Within the nucleus of an atom are specific numbers of positively charged protons (p^+) and uncharged neutrons (n^0). The negatively charged electrons (e^-) are around the nucleus. The atoms depicted here are electrically neutral because the number of protons and number of electrons within each atom are equal. (*b*) Electrons occupy separate electron shells. A maximum of two electrons can occupy the innermost shell closest to the nucleus; all other shells contain a maximum of eight electrons.

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Each element is uniquely defined by the number of protons in the atoms of that element. For example, only hydrogen atoms have one proton, only carbon atoms have six protons, and only oxygen atoms have eight protons (figure 2.1; see table 2.1). The number of protons in each atom is called the **atomic number,** and because the number of electrons and protons in an atom are equal, the atomic number is also the number of electrons.

Protons and neutrons have about the same mass, and they are responsible for most of the mass of atoms. Electrons, on the other hand, have very little mass. The **mass number** of an element is determined by adding the number of protons and neutrons in each atom. For example, because carbon has 6 protons and 6 neutrons, its mass number is 12 $(6 + 6 = 12)$.

Understand ***Apply It 2***

The atomic number of fluorine is 9, and the mass number is 19. What is the number of protons, neutrons, and electrons in an atom of fluorine?

Isotopes

Isotopes are two or more forms of the same element that have the same number of protons and electrons, but have a different number of neutrons. The most familiar isotopes are those that are radioactive, which are used in nuclear medicine and other applications. For example, a positron emission tomography (PET) scan uses radioactive isotopes to examine blood flow to certain organs or to detect cancer.

Electrons and Chemical Bonding

Recall from chapter 1 that the simplest level of organization is the chemical level. This level is the interaction between atoms to form molecules by either sharing or transferring their outermost electrons. In doing so, these atoms form **chemical bonds.**

The chemical behavior of an atom is dependent on its electrons. The electron cloud around an atom's nucleus is organized into different energy levels depending on the distance of an electron from the nucleus. For simplicity, the energy levels are often drawn as concentric rings, called **electron shells,** around the nucleus (see figure 2.1*b*). There is a maximum number of electrons that each shell can hold. Outer shells do not contain electrons until the inner shells have reached their maximum. The innermost shell (the shell closest to the nucleus) holds a maximum of 2 electrons, and the remaining shells hold a maximum of 8 electrons. The outermost shell is called the **valence shell.** The number of electrons in the valence shell determines an atom's chemical behavior. If an atom's valence shell is not at its maximum, it will form bonds with other atoms to achieve a full valence shell, called an octet. Thus, most atoms follow the **octet rule**—the tendency of atoms to combine with other atoms until each has 8 electrons (2 electrons for hydrogen) in its valence shell.

Atoms achieve an octet in one of two ways: (1) by transferring electrons between atoms or (2) by sharing electrons between atoms. The fate of electrons as being either transferred or shared determines the type of chemical bond: ionic or covalent, as discussed in the next sections.

Whether an electron is transferred or shared between two atoms is determined by the relative electronegativities of the two atoms. **Electronegativity** is the ability of the atom's nucleus to pull electrons toward it. Atoms with a strong electronegativity are those with 6 or 7 electrons in the valence shell—these are very close to achieving an octet. Atoms with a weak electronegativity are those with only 1 or 2 electrons in the valence shell—these are farther away from achieving an octet. The notable exception to this generalization is hydrogen. Because hydrogen only has 1 proton in its nucleus, its electronegativity is lower than that of other, larger atoms that lack only one valence electron.

In a chemical bond, the fate of the electrons between two atoms depends on the relative difference in electronegativity between the atoms. When they are very different, the atoms tend to transfer electrons from one atom to the other. However, when the electronegativities are similar, the atoms are likely to share the electrons. For example, an atom with 7 electrons in its valence shell has a strong pull on electrons, whereas an atom with 1 electron in its valence shell has a weak pull on electrons. Thus, the "strong" atom can "steal" the valence electron from the "weak"

atom, resulting in a transfer of electrons. The relationship between electronegativity and the resultant chemical bond types is illustrated in figure 2.2. The two major types of chemical bonds are ionic and covalent bonds.

Figure 2.2 **Relationship Between Electronegativity and Chemical Bonding**

Electronegativity is a measure of how much an atom attracts electrons from another atom to form a chemical bond. Covalent bonds are formed by the sharing of electrons between atoms that have the same electronegativity (nonpolar covalent bond; e.g., H_2) or a relatively small difference in electronegativities (polar covalent bonding; e.g., H_2O). Ionic bonds are formed by the transfer of electrons between two atoms that have very different electronegativities (e.g., NaCl).

Ionic Bonding

Recall that an atom is electrically neutral because it has an equal number of protons and electrons. However, depending on its electronegativity, an atom can donate electrons to or gain electrons from other atoms. When this occurs, the numbers of protons and electrons are no longer equal, and a charged particle called an **ion** (EYE-on) is formed. After a weakly electronegative atom loses an electron, it has one more proton than it has electrons and is positively charged. A sodium atom (Na) can lose an electron to become a positively charged sodium ion (Na^+) (figure 2.3*a*). After an atom gains an electron, it has one more electron than it has protons and is negatively charged. A chlorine atom (Cl) can accept an electron to become a negatively charged chloride ion (Cl^-). After this transfer of electrons, both chlorine and sodium have full valence shells.

Figure 2.3 APR **Ionic Bonding**

(*a*) A sodium atom (Na) loses an electron to become a smaller, positively charged ion, and a chlorine atom (Cl) gains an electron to become a larger, negatively charged ion. The attraction between the oppositely charged ions results in ionic bonding and the formation of sodium chloride. (*b*) The Na^+ and Cl^- are organized to form a cube-shaped array. (*c*) A photomicrograph of salt crystals reflects the cubic arrangement of the ions.

(c) ©Trent Stephens

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Because oppositely charged ions are attracted to each other, negatively charged ions and positively charged ions tend to remain close together. Thus an **ionic** (eye-ON-ik) bond forms when electrons are transferred between atoms, creating oppositely charged ions. For example Na^+ and Cl^- are held together by ionic bonding to form an array of ions called sodium chloride (NaCl), or table salt (figure 2.3*b*,*c*). Table 2.2 lists some ions commonly found in the body.

Table 2.2 Important Ions in the Human Body

Ion	Symbol	Significance*
Calcium	Ca^{2+}	Part of bones and teeth; functions in blood clotting, muscle contraction, release of neurotransmitters
Sodium	Na^+	Membrane potentials, water balance
Potassium	K^+	Membrane potentials
Hydrogen	H^+	Acid-base balance
Hydroxide	OH^-	Acid-base balance
Chloride	Cl^-	Water balance
Bicarbonate	HCO_3^-	Acid-base balance
Ammonium	NH_4^+	Acid-base balance
Phosphate	PO_4^{3-}	Part of bones and teeth; functions in energy exchange, acid-base balance
Iron	Fe^{2+}	Red blood cell function
Magnesium	Mg^2	Necessary for enzymes
Iodide	I^-	Present in thyroid hormones

*The ions are part of the structures or play important roles in the processes listed.

Understand **Apply It 3**

If an iron (Fe) atom loses three electrons, what is the charge of the resulting ion? Write the symbol for this ion.

Covalent Bonding

A **covalent bond** forms when atoms share one or more pairs of electrons. The sharing of electrons, rather than the transfer of electrons, occurs because the atoms have similar electronegativities. The resulting combination of atoms is called a

molecule (MOLL-eh-kyul). Figure 2.4*a* illustrates the formation of a covalent bond between two hydrogen atoms to form a hydrogen molecule.

❶ Initially the two atoms do not interact, because they are too far apart. Each hydrogen atom has 1 electron.

❷ As the atoms get closer together, each hydrogen atom's positively charged nucleus begins to attract the electron of the other hydrogen atom.

❸ A **nonpolar** covalent bond forms when the electrons are shared equally between the nuclei, because the electrons have the same attraction to each nucleus (figure 2.4*b*). The two hydrogen atoms are held together by a nonpolar covalent bond and now form a **nonpolar molecule**.

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PROCESS Figure

PROCESS Figure 2.4 **Nonpolar Covalent Bonds**

(*a*) In a nonpolar bond, there is an even distribution of electrons due to the equal electronegativities of the two atoms. (*b*) Molecules formed by nonpolar covalent bonds are neutral. The electron distribution (arrow) is equal between the two nuclei.

What type of bond would form when electrons are shared between an atom with stronger electronegativity and an atom with weaker electronegativity?

However, the sharing of electrons between atoms does not always result in a nonpolar covalent bond. In cases where the two atoms involved in a covalent bond have different electronegativities, **polar covalent bonds** will form (see figure 2.5). Polar covalent bonds can result in **polar molecules,** which are electrically asymmetric. For example, oxygen atoms have a higher electronegativity than do hydrogen atoms. When covalent bonding between an oxygen atom and two hydrogen atoms forms a water molecule, the electron cloud is closer to the oxygen nucleus than to the hydrogen nuclei. Because electrons have a negative charge, the oxygen side of the molecule is slightly more negative than the hydrogen side (figure 2.6).

Molecules and Compounds

A molecule is formed when two or more atoms chemically combine to form a structure that behaves as an independent unit. Sometimes the atoms that combine are of the same type, as when two hydrogen atoms combine to form a hydrogen molecule. But more typically, a molecule consists of two or more different types of atoms, such as two hydrogen atoms and an oxygen atom combining to form water. Thus, a glass of water consists of a collection of individual water molecules positioned next to one another.

A **compound** (KOM-pound; to place together) is a substance resulting from the chemical combination of two or more *different* types of atoms. Water is an example of a substance that is a compound and a molecule. Not all molecules are compounds. For example, a hydrogen molecule is not a compound because it does not consist of different types of atoms.

Some compounds are molecules and some are not. (Remember that to be a molecule, a structure must be an independent unit.) Covalent compounds, in which different types of atoms are held together by covalent bonds, are molecules because the sharing of electrons results in distinct units. On the other hand, ionic compounds, in which ions are held together by the force of attraction between opposite charges, are not molecules because they do not consist of distinct units. Sodium chloride is an example of a substance that is a compound but not a molecule. A piece of sodium chloride does not consist of individual sodium chloride molecules positioned next to one another. Instead, it is an organized array of individual Na^+ and individual Cl^- in which each charged ion is surrounded by several ions of the opposite charge (see figure 2.3*b*).

Intermolecular force (hydrogen bond)
Atom
Water molecule
Hydrogen bond
Hydrogen
Oxygen
δ−
e⁻ pull
e⁻ pull
Polar covalent bond
δ+
δ+
(a)
Higher electron density

(b)

Figure 2.5 **Polar Covalent Bonds**

(*a*) A water molecule forms when one oxygen atom forms polar covalent bonds with two hydrogen atoms. In a polar covalent bond, such as with water, there is an uneven distribution of electrons due to the stronger electronegativity of oxygen compared to that of hydrogen. This creates charged regions of the molecule. The oxygen side of the molecule has a slight negative charge (*indicated by* δ^-), and the hydrogen side of the molecule has a slight positive charge (*indicated by* δ^+). (*b*) Molecules formed by polar covalent bonds have charged portions. The electron distribution is unequal between two nuclei and the electron density is greater around the nucleus with the stronger electronegativity.

Figure 2.6 **Hydrogen Bonds**

The positive hydrogen part of one water molecule (δ^+) forms a hydrogen bond (*dotted line*) with the negative oxygen part of another water molecule (δ^-). As a result, hydrogen bonds hold separate water molecules together.

Molecules and compounds can be represented by the symbols of the atoms forming the molecule or compound plus subscripts denoting the quantity of each type of atom present. For example, glucose (a sugar) can be represented as $C_6H_{12}O_6$, indicating that glucose is composed of 6 carbon, 12 hydrogen, and 6 oxygen atoms. Letter symbols represent most atoms and molecules. Throughout this chapter and the text, oxygen (O_2), carbon dioxide (CO_2), and other commonly discussed ions and molecules will be identified by their symbols when appropriate.

Intermolecular Forces

Intermolecular forces are the weak charge attractions that exist between separate molecules, or between ions and molecules. These intermolecular forces are different from other chemical bonds in that there is no exchange of electrons. Because these attractions are between already-formed molecules, any electron exchange has already occurred. Intermolecular forces are simply due to attractions between oppositely charged regions of molecules and include hydrogen bonds and the property of dissociation.

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Hydrogen Bonds

Molecules with polar covalent bonds have positive and negative "ends." Intermolecular force results from the attraction of the positive end of one polar molecule to the negative end of another polar molecule. For example, when hydrogen forms a covalent bond with oxygen, nitrogen, or fluorine, the resulting molecule becomes very polarized. If the positively charged hydrogen of one molecule is attracted to the negatively charged oxygen, nitrogen, or fluorine of another molecule, a **hydrogen bond** forms. A common example of hydrogen bonding occurs between water molecules and other polar molecules (figure 2.6). These hydrogen bonds are essential for several unique properties of water. Consider the attraction of water molecules to each other when answering this chapter's Learn to Apply It question.

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In addition to intermolecular bonds between water molecules, hydrogen bonds form intramolecular bonds within the same molecule. Intramolecular hydrogen bonds form the more complex structure of proteins and nucleic acids and help stabilize their final three-dimensional shapes (see section 2.5).

Table 2.3 summarizes the important characteristics of chemical bonds (ionic and covalent) and forces between separate molecules (hydrogen bonds).

Table 2.3 Comparison of Bonds

Bonds Between Atoms	Example

Bonds Between Atoms	Example
Ionic Bond A complete transfer of electrons between two atoms results in separate positively charged and negatively charged ions.	Na^+Cl^- Sodium chloride
Polar Covalent Bond An unequal sharing of electrons between two atoms results in a slightly positive charge (δ^+) on one side of the molecule and a slightly negative charge (δ^-) on the other side of the molecule.	 Water
Nonpolar Covalent Bond An equal sharing of electrons between two atoms results in an even charge distribution among the atoms of the molecule.	 Methane
Bonds Between Molecules	**Example**
Hydrogen Bond The attraction of oppositely charged ends of one polar molecule to another polar molecule holds molecules or parts of molecules together.	 Water molecules

Dissociation

When ionic compounds dissolve in water, their ions **dissociate** (DISS-so-see-ate), or separate, from each other because the positively charged ions are attracted to the negative ends of the water molecules, and the negatively charged ions are attracted to the positive ends of the water molecules. For example, when sodium chloride dissociates in water, the Na^+ and Cl^- separate and water molecules surround and isolate the ions, keeping them in solution (figure 2.7). These dissociated ions are sometimes called **electrolytes** (ee-LEK-troh-lytes) because they have the capacity to conduct an electrical current, the flow of charged particles. For example, an electrocardiogram (ECG) is a recording of electrical currents produced by the heart. These currents can be detected by electrodes on the surface of the body because the ions in the body fluids conduct electrical currents.

Figure 2.7 APR **Dissociation**

Sodium chloride (table salt) dissociates in water. The positively charged Na^+ are attracted to the negatively charged oxygen (δ^-) end of the water molecule, and the negatively charged Cl^- are attracted to the positively charged hydrogen (δ^+) end of the water molecule.

When molecules dissolve in water, the molecules usually remain intact even though they are surrounded by water molecules. Thus, in a glucose solution, glucose molecules are surrounded by water molecules.

2.2 CHEMICAL REACTIONS AND ENERGY

Learning Outcomes *After reading this section, you should be able to*

A. Summarize the characteristics of synthesis, decomposition, and exchange reactions.
B. Explain how reversible reactions produce chemical equilibrium.
C. Distinguish between chemical reactions that release energy and those that take in energy.
D. Describe the factors that can affect the rate of chemical reactions.

A **chemical reaction** is the formation or breaking of chemical bonds between atoms, ions, molecules, or compounds. The substances that enter into a chemical reaction are called the **reactants,** and the substances that result from the chemical reaction are called the **products.**

Classification of Chemical Reactions

For our purposes, chemical reactions can be classified as synthesis, decomposition, or exchange reactions.

Synthesis Reactions

When two or more reactants combine to form a larger, more complex product, the process is called a **synthesis reaction,** represented symbolically as

$$A + B \rightarrow AB$$

Examples of synthesis reactions include the synthesis of the complex molecules of the human body from the basic "building blocks" obtained in food and the synthesis of **adenosine triphosphate (ATP)** (ah-DEN-o-seen try-FOS-fate) molecules. In ATP, *A* stands for adenosine, *T* stands for *tri-* (or three), and *P* stands for a phosphate group (PO_4^{3-}). Thus, ATP consists of adenosine and three phosphate groups. ATP is synthesized when adenosine diphosphate (ADP), which has two (*di-*) phosphate groups, combines with a phosphate group to form the larger ATP molecule. The phosphate group that reacts with ADP is often denoted as P_i, where the *i* indicates that the phosphate group is associated with an inorganic substance (see "Inorganic Molecules" later in this chapter).

A-P-P	+	P_i	→	A-P-P-P
(ADP)		(Phosphate group)		(ATP)

All of the synthesis reactions that occur in the body are collectively referred to as **anabolism** (an-AB-oh-lizm). Another example of a synthesis reaction is the linking of building blocks to form proteins, which results in water formation. Synthesis reactions in which water is also a product are called **dehydration** (water-out) **reactions**. Growth, maintenance, and repair of the body could not take place without anabolic reactions.

Decomposition Reactions

In a **decomposition reaction,** reactants are broken down into smaller, less complex products. A decomposition reaction is the reverse of a synthesis reaction and can be represented in this way:

$$AB \rightarrow A + B$$

Examples of decomposition reactions include the breakdown of food molecules into basic building blocks and the breakdown of ATP to ADP and a phosphate group.

A-P-P-P	→	A-P-P	+	P_i
(ATP)		(ADP)		(Phosphate group)

The decomposition reactions that occur in the body are collectively called **catabolism** (kah-TAB-oh-lizm). Another example of a decomposition reaction is the

breakdown of foods into individual nutrients, which uses water in the process. Reactions that use water in this way are called **hydrolysis** (high-DROL-ih-sis; water-breakdown) **reactions.** They include the digestion of food molecules in the intestine and within cells, the breakdown of lipid stores, and the breakdown of foreign matter and microorganisms in certain blood cells that protect the body. All of the anabolic and catabolic reactions in the body are collectively defined as **metabolism.**

Exchange Reactions

An **exchange reaction** is a combination of a decomposition reaction and a synthesis reaction. In decomposition, the reactants are broken down. In synthesis, the products of the decomposition reaction are combined. The symbolic representation of an exchange reaction is

$$\mathrm{AB} + \mathrm{CD} \rightarrow \mathrm{AC} + \mathrm{BD}$$

An example of an exchange reaction is the reaction of hydrochloric acid (HCl) with sodium hydroxide (NaOH) to form table salt (NaCl) and water (H_2O):

$$\mathrm{HCl} + \mathrm{NaOH} \rightarrow \mathrm{NaCl} + \mathrm{H_2O}$$

Reversible Reactions

In a **reversible reaction,** the reaction can run in the opposite direction, so that the products are converted back to the original reactants. When the rate of product formation is equal to the rate of reactant formation, the reaction is said to be at **equilibrium.** At equilibrium, the amount of the reactants relative to the amount of products remains constant.

The following analogy may help clarify the concept of reversible reactions and equilibrium. Imagine a trough containing water. The trough is divided into two compartments by a partition, but the partition contains holes that allow the water to move freely between the compartments. Because the water can move in either direction, this is like a reversible reaction. The amount of water in the left compartment represents the amount of reactant, and the amount of water in the right compartment represents the amount of product. At equilibrium, the amount of reactant relative to the amount of product in each compartment is always the same because the partition allows water to pass between the two compartments until the level of water is the same in both compartments. If the amount of reactant is increased by adding water to the left compartment, water flows from the left compartment through the partition to the right compartment until the level of water is the same in both. Thus, the amounts of reactant and product are once again equal. Unlike this analogy, however, the amount of reactant relative to the amount of product in most reversible reactions is not one to one. Depending on the specific

reversible reaction, there can be one part reactant to two parts product, two parts reactant to one part product, or many other possibilities.

An important reversible reaction in the human body occurs when carbon dioxide (CO_2) and water (H_2O) form hydrogen ions (H^+) and bicarbonate ions (HCO_3^-). The reversibility of the reaction is indicated by two arrows pointing in opposite directions:

$$CO_2 + H_2O \rightleftarrows H^+ + HCO_3^-$$

If CO_2 is added to H_2O, the amount of CO_2 relative to the amount of H^+ increases. However, the reaction of CO_2 with H_2O produces more H^+, and the amount of CO_2 relative to the amount of H^+ returns to equilibrium. Conversely, adding H^+ results in the formation of more CO_2, and the equilibrium is restored.

Maintaining a constant level of H^+ in body fluids is necessary for the nervous system to function properly. This level can be maintained, in part, by controlling blood CO_2 levels. For example, slowing the respiration rate causes blood CO_2 levels to increase, which causes an increase in H^+ concentration in the blood.

Understand **Apply It 4**

If the respiration rate increases, CO_2 is removed from the blood. What effect does this have on blood H^+ levels?

Energy

Energy is defined as the capacity to do **work.** So, what is the definition of work? Work is the movement of matter. That means that *energy is the ability to put matter into motion*. In this straightforward definition of energy, you can clearly see the importance of *understanding* a definition, rather than simply *memorizing* it. Energy can be subdivided into potential energy and kinetic energy. **Potential energy** is stored energy. **Kinetic** (ki-NET-ik; of motion) **energy** is energy caused by the movement of an object and is the form of energy that actually does work. A ball held at arm's length above the floor has potential energy. No energy is expended as long as the ball does not move. However, if the ball is released and falls toward the floor, it has kinetic energy. When potential energy is released, it becomes kinetic energy, thus doing work.

Potential and kinetic energy exist in many different forms: mechanical energy, chemical energy, heat energy, electrical energy, and electromagnetic (radiant) energy. In this text, we will consider mechanical energy and chemical energy in more detail than the other forms of energy. **Mechanical energy** is energy resulting from the position or movement of objects. Many of the activities of the human body, such as moving a limb, breathing, or circulating blood, involve mechanical energy. According to the law of conservation of energy, the total energy of the universe is constant. Therefore, energy is neither created nor destroyed, but it can take on different forms. For example, the potential energy in the ball is converted into kinetic energy as the

ball falls toward the floor. Conversely, the kinetic energy required to raise the ball from the floor is converted back into potential energy.

Chemical energy is a form of potential energy stored within the chemical bonds of a substance. In any chemical reaction, the potential energy within the chemical bonds of the reactants can be compared with the potential energy in the chemical bonds of the products. If the potential energy in the reactants is *less* than that in the products, energy input is needed for the reaction to occur. An example is the synthesis of ATP from ADP:

ADP	+	P_i	+	Energy	→	ATP
(less potential energy in reactants)				from food molecules		(more potential energy in products)

For clarity, P_i is used to represent inorganic phosphate. As a result of breaking of existing chemical bonds in food molecules, new chemical bonds are formed to create ATP. It is the release of energy from the breaking of bonds and the formation of new bonds that allow these products to have more potential energy than the reactants (figure 2.8*a*).

Figure 2.8 APR **Energy and Chemical Reactions**

In the two reactions shown here, the larger "sunburst" represents greater potential energy and the smaller "sunburst" represents less potential energy. (*a*) The input of energy is required for the synthesis of ATP. (*b*) Energy is released as a result of the breakdown of ATP.

If the potential energy in the reactants is *more* than that in the products, energy is released from this reaction. For example, the breakdown of ATP releases energy:

ATP	→	ADP	+	P_i	+	Energy
(more potential energy in products)		(less potential energy in reactants)				used by cells

The majority of this energy released is used by cells to do work such as synthesizing or transporting certain molecules in the cell, or to do mechanical work such as contracting muscles (figure 2.8*b*). Some energy from the breakdown of ATP is released as heat. Human body temperature is maintained by heat produced as a by-product of chemical reactions.

Understand ***Apply It 5***

Why does body temperature increase during exercise?

Rate of Chemical Reactions

The rate at which a chemical reaction proceeds is influenced by several factors. At normal body temperatures, most chemical reactions would take place too slowly to sustain life—if not for substances called catalysts. A **catalyst** (KAT-uh-list) increases the rate of a chemical reaction, without itself being permanently changed or depleted. Many of the chemical reactions that occur in the body require enzymes. An **enzyme** (EN-zime) is a protein catalyst that increases the rate at which a chemical reaction proceeds, without the enzyme being permanently changed. Many, but not all, enzymes have been given names that end with the suffix *-ase*. Enzymes increase the rate of chemical reactions by lowering the activation energy, which is the energy necessary to start a chemical reaction. Even reactions that release energy must overcome the activation energy barrier for the reaction to occur. For example, heat in the form of a spark is required to start the reaction between O_2 and gasoline vapor. Once some oxygen molecules react with gasoline vapor, the energy released can start additional reactions. Most of the chemical reactions that occur in the body have high activation energies, which are decreased by enzymes (figure 2.9). The lowered activation energies enable reactions to proceed at rates that sustain life.

Figure 2.9 **Activation Energy and Enzymes**

Activation energy (E_A) is required to initiate chemical reactions. Without an enzyme, a chemical reaction can proceed, but it needs more energy input. Enzymes lower the activation energy, making it easier for the reaction to proceed.

CLINICAL IMPACT

Applications of Atomic Particles

Protons, neutrons, and electrons are responsible for the chemical properties of atoms. They also have other properties that can be useful in a clinical setting. For example, they have been used to develop methods for examining the inside of the body.

X-rays are electromagnetic radiations with a much shorter wavelength than visible light. When electric current is used to heat a filament to very high temperatures, the energy of the electrons becomes so great that some electrons are emitted from the hot filament. When these electrons strike a positive electrode at high speeds, they release some of their energy in the form of x-rays.

X-rays do not penetrate dense material as readily as they penetrate less dense material, and x-rays can expose photographic film. Consequently, an x-ray beam can pass through a person and onto photographic film. Dense tissues of the body absorb the x-rays; on the film, these areas are underexposed and, so, appear white or light in color. By contrast, the x-rays readily pass through less dense tissue, so the film in these areas is overexposed and they appear black or dark in color. In an x-ray film of the skeletal system, the dense bones are white, and the less dense soft tissues are dark, often so dark that no details can be seen. Health professionals use x-rays to determine whether bones are broken or have other abnormalities.

Soft tissues can be photographed by using low-energy x-rays. Mammograms are low-energy x-rays of the breast that can reveal tumors because tumors are slightly denser than normal tissue.

Radiopaque substances are dense materials that absorb x-rays. If a radiopaque liquid is given to a patient, the liquid assumes the shape of the organ into which it is placed. For example, if a patient swallows a barium solution, the outline of the upper digestive tract can be photographed using x-rays to detect any abnormality, such as an ulcer.

Within limits, the greater the concentration of the reactants, the greater the rate at which a chemical reaction will occur because, as the concentration increases, the reacting molecules are more likely to come in contact with one another. For example, the normal concentration of O_2 inside cells enables it to come in contact with other molecules, producing the chemical reactions necessary for life. If the O_2 concentration decreases, the rate of chemical reactions decreases. A decrease in O_2 in cells can impair cell function and even result in death.

Because molecular motion changes as environmental temperature changes, the rate of chemical reactions is partially dependent on temperature. For example, reactions occur throughout the body at a faster rate when a person has a fever of only a few degrees. The result is increased activity in most organ systems, such as increased heart and respiratory rates. Conversely, when body temperature drops, the fingers are not as agile, largely because of the reduced rate of chemical reactions in cold muscle tissue.

2.3 ACIDS AND BASES

Learning Outcomes *After reading this section, you should be able to*

A. Describe the pH scale and its relationship to acidic and basic solutions.
B. Explain the importance of buffers in organisms.

The body has many molecules and compounds, called acids and bases, that can alter body functions. An **acid** is a proton donor. Because a hydrogen atom without its electron is a proton, any substance that releases hydrogen ions (H^+) in water is an acid. For example, hydrochloric acid (HCl) in the stomach forms H^+ and chloride ions (Cl^-):

$$HCl \rightarrow H^+ + Cl^-$$

A **base** is a proton acceptor. For example, sodium hydroxide (NaOH) forms sodium ions (Na^+) and hydroxide ions (OH^-). It is a base because the OH^- is a proton acceptor that binds with a H^+ to form water.

The pH Scale

The **pH scale** is a means of referring to the H^+ concentration in a solution (figure 2.10). The concentration of H^+ determines the pH value. The scale ranges from 0 to 14. A **neutral solution** has an equal number of H^+ and OH^- and thus a pH of 7.0. An **acidic solution** has a greater concentration of H^+ than of OH^- and thus a pH *less* than 7.0. A **basic,** or *alkaline* (AL-kah-line), **solution** has fewer H^+ than OH^- and thus a pH *greater* than 7.0. Notice that the pH number and the actual H^+

concentration are inversely related, meaning that the lower the pH number, the higher the H^+ concentration.

(a)

	Concentration H^+ (moles/liter)		pH
High H^+	1	(1×10^{0})	0
	0.1	(1×10^{-1})	1
	0.01	(1×10^{-2})	2
	0.001	(1×10^{-3})	3
	0.0001	(1×10^{-4})	4
	0.00001	(1×10^{-5})	5
	0.000001	(1×10^{-6})	6
	0.0000001	(1×10^{-7})	7
	0.00000001	(1×10^{-8})	8
	0.000000001	(1×10^{-9})	9
	0.0000000001	(1×10^{-10})	10
	0.00000000001	(1×10^{-11})	11
	0.000000000001	(1×10^{-12})	12
	0.0000000000001	(1×10^{-13})	13
Low H^+	0.00000000000001	(1×10^{-14})	14

(b)

Figure 2.10 **pH Scale**

(*a*) A pH of 7 is considered neutral. Higher acidity (higher concentration of H^+) causes a lower pH, so that values less than 7 are acidic (the lower the number, the more acidic). Lower acidity (lower concentration of H^+) causes a higher pH, so that values greater than 7 are basic (the higher the number, the more basic). Representative fluids and their approximate pH values are listed. (*b*) Correlation of pH and hydrogen ion concentrations shown in decimal form and scientific notation.

As the pH value becomes smaller, the solution becomes more acidic; as the pH value becomes larger, the solution becomes more basic. A change of one unit on the pH scale represents a 10-fold change in the H^+ concentration. For example, a solution with a pH of 6.0 has 100 times more H^+ than a solution with a pH of 8.0. Thus, small changes in pH represent large changes in H^+ concentration. Think about the

relationship between pH number and H^+ concentration. Using dots to represent H^+, draw two areas, one with high pH and one with low pH. Does the one with high pH have fewer dots? If so, you have a good understanding of a rather difficult concept.

The normal pH range for human blood is 7.35 to 7.45. If blood pH drops below 7.35, a condition called **acidosis** (ass-ih-DOH-sis) results. The nervous system is depressed, and the individual becomes disoriented and possibly comatose. If blood pH rises above 7.45, **alkalosis** (al-kah-LO-sis) results. The nervous system becomes overexcitable, and the individual can be extremely nervous or have convulsions. Both acidosis and alkalosis can result in death.

Salts

A **salt** is a compound consisting of a positive ion other than H^+ and a negative ion other than OH^-. Salts are formed by the reaction of an acid and a base. For example, hydrochloric acid (HCl) combines with sodium hydroxide (NaOH) to form the salt sodium chloride (NaCl):

$$\underset{\text{(Acid)}}{HCl} + \underset{\text{(Base)}}{NaOH} \rightarrow \underset{\text{(Salt)}}{NaCl} + \underset{\text{(Water)}}{H_2O}$$

Buffers

The chemical behavior of many molecules changes as the pH of the solution in which they are dissolved changes. The survival of an organism depends on its ability to maintain homeostasis by keeping body fluid pH within a narrow range. One way normal body fluid pH is maintained is through the use of buffers. A **buffer** (BUFF-er) is a chemical that resists changes in pH when either an acid or a base is added to a solution containing the buffer (figure 2.11).

Figure 2.11 **Buffers**

(*a*) The addition of an acid to a nonbuffered solution of water results in an increase of H^+ that causes a large decrease in pH. (*b*) The addition of an acid to a buffered solution results in a much smaller change in pH. The added H^+ bind to the buffer (symbolized by the letter *B*).

❶ When an acid is added to an unbuffered water solution, the result is increased H^+ and decreased pH.

❷ Buffers reduce large changes in pH by binding and releasing H^+.

❸ When an acid is added to a buffered solution, the buffer binds to the H^+, preventing these ions from causing a decrease in the pH of the solution.

Understand

Apply It 6

If a base is added to a solution, will the pH of the solution increase or decrease? If the solution is buffered, what response from the buffer prevents the change in pH?

2.4 INORGANIC MOLECULES

Learning Outcomes *After reading this section, you should be able to*

A. Distinguish between inorganic and organic molecules.

B. Describe how the properties of O_2, CO_2, and water contribute to their physiological functions.

Inorganic chemistry generally deals with substances that do not contain carbon, although a more rigorous definition is that it deals with substances that lack carbon-hydrogen bonds. **Organic chemistry** is the study of carbon-containing substances, with a few exceptions. For example, CO_2 and carbon monoxide (CO) are important inorganic substances that contain carbon, but lack carbon-hydrogen bonds.

In this section, we discuss the important roles of inorganic molecules in human anatomy and physiology. Inorganic substances play many vital roles in human anatomy and physiology. Examples include (1) the O_2 we breathe, (2) the CO_2 we exhale, (3) the calcium phosphate that makes up our bones, and (4) metals required for protein functions, such as iron for O_2 transport.

Oxygen and Carbon Dioxide

Oxygen (O_2) is a small, nonpolar, inorganic molecule consisting of two oxygen atoms bound together by a double covalent bond. About 21% of the gas in the atmosphere is O_2, and it is essential for most living organisms. Humans require O_2 in the final step of a series of chemical reactions in which energy is extracted from food molecules (see chapter 17).

Carbon dioxide (CO_2) consists of one carbon atom bound to two oxygen atoms. Each oxygen atom is bound to the carbon atom by a double covalent bond. Carbon dioxide is produced when food molecules, such as glucose, are metabolized within the cells of the body. Once CO_2 is produced, it is eliminated from the cell as a metabolic by-product, transferred to the lungs by the blood, and exhaled during respiration. If CO_2 is allowed to accumulate within cells, it becomes toxic.

Water

Water has many unique properties due to its polar nature. Recall that a molecule of water is formed when an atom of oxygen forms polar covalent bonds with two atoms of hydrogen. Because of water's polarity, other polar molecules, including other water molecules, are attracted to it. Molecules that are attracted to water are call **hydrophilic** (hye-droh-FIL-ik). In contrast, molecules that lack this attraction are called **hydrophobic** (hye-droh-FOH-bik).

As previously discussed, it is water's polarity and the attraction to other water molecules that is responsible for the formation of hydrogen bonds between adjacent water molecules. The hydrogen bonds contribute to those properties of water that make water necessary for life:

1. *Water stabilizes body temperature.* Because heat energy causes not only movement of water molecules, but also disruption of hydrogen bonds, water can absorb large amounts of heat and remain at a stable temperature. Blood, which is mostly water, is warmed deep in the body and then flows to the surface, where the heat is released. In addition, water evaporation in the form of sweat results in significant heat loss from the body. This information may be helpful to you when you answer this chapter's Learn to Apply It question.
2. *Water protects the body.* Water is an effective lubricant. For example, tears protect the surface of the eye from the rubbing of the eyelids. Water also forms a fluid cushion around organs, which helps protect them from damage. For example, your brain is protected by a fluid that surrounds it and separates it from the bones of your skull.
3. *Water is required for many chemical reactions.* Most of the chemical reactions necessary for life do not take place unless the reacting molecules are dissolved in water. For example, NaCl must dissociate in water into Na^+ and Cl^- before those ions can react with other ions. Water also directly participates in many chemical reactions. For example, during the digestion of food, large molecules and water react to form smaller molecules.

2.5 ORGANIC MOLECULES

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the structural organization and major functions of carbohydrates, lipids, proteins, and nucleic acids.
B. Explain how enzymes work.
C. Describe the role of nucleotides in the structure and function of ATP.

Carbon's ability to form covalent bonds with other atoms makes possible the formation of the large, diverse, complicated molecules necessary for life. These are called organic molecules, or sometimes biomolecules. Our cells utilize organic molecules for many purposes, some of which include: (1) as energy molecules for synthesis of ATP, (2) as structural components of the cell, and (3) as regulatory molecules. Carbon atoms bound together by covalent bonds constitute the "backbone" of many large molecules. Two mechanisms that allow the formation of a wide variety of molecules are (1) variation in the length of the carbon chains and (2) the combination of the atoms involved. For example, some protein molecules have thousands of carbon atoms bound by covalent bonds to one another and to other atoms, such as nitrogen, sulfur, hydrogen, and oxygen.

The four major groups of organic molecules essential to living organisms are (1) carbohydrates, (2) lipids, (3) proteins, and (4) nucleic acids. Each of these groups has specific structural and functional characteristics (table 2.4).

Table 2.4 Important Organic Molecules and Their Functions in the Body

Molecule	Elements	Building Blocks	Function	Examples
Carbohydrate	C, H, O	Monosaccharides	Energy	Monosaccharides can be used as energy sources. Glycogen (a polysaccharide) is an energy-storage molecule.
Lipid	C, H, O (P, N in some)	Glycerol and fatty acids (for fats)	Energy	Fats can be stored and broken down later for energy; per unit of weight, fats yield twice as much energy as carbohydrates.
			Structure	Phospholipids and cholesterol are important components of cell membranes. Adipose tissue surrounds organs to protect them.
			Regulation	Steroid hormones regulate many physiological processes (e.g., estrogen and testosterone are responsible for many of the differences between males and females).
Protein	C, H, O, N (S in most)	Amino acids	Regulation	Enzymes control the rate of chemical reactions. Hormones regulate many physiological processes (e.g., insulin affects glucose transport into cells).
			Structure	Collagen fibers form a structural framework in many parts of the body.
			Energy	Proteins can be broken down for energy; per unit of weight, they yield the same energy as carbohydrates.
			Contraction	Actin and myosin in muscle are responsible for muscle contraction.
			Transport	Hemoglobin transports O_2 in the blood.
			Protection	Antibodies and complement protect against microorganisms and other foreign substances.
Nucleic acid	C, H, O, N, P	Nucleotides	Regulation	DNA directs the activities of the cell.
			Heredity	Genes are pieces of DNA that can be passed from one generation to the next.

Molecule	Elements	Building Blocks	Function	Examples
			Gene expression	RNA is involved in gene expression.

Carbohydrates

Carbohydrates are organic molecules composed of carbon, hydrogen, and oxygen atoms. Carbohydrates have three major roles in the body (table 2.4): (1) they are parts of other organic molecules, (2) they are broken down to provide energy, and (3) when undigested, they provide bulk (fiber) in feces. In most carbohydrates, for each carbon atom there are two hydrogen atoms and one oxygen atom. Note that this two-to-one ratio is the same as in water (H_2O). The molecules are called carbohydrates because each carbon (*carbo-*) is combined with the same atoms that form water (*hydrated*). For example, the chemical formula for glucose is $C_6H_{12}O_6$.

The simplest carbohydrates are **monosaccharides** (MON-oh-SACK-ah-rides; *mono*, one), or simple sugars. Monosaccharides are considered the building blocks of carbohydrates because larger, more complex carbohydrates are formed by covalent bonds that link many monosaccharides together. Glucose (blood sugar) and fructose (fruit sugar) are important monosaccharide energy sources for many of the body's cells. In fact, cells preferentially use glucose to synthesize ATP.

Disaccharides (die-SACK-ah-rides; *di*, two) are formed when two monosaccharides are joined by a covalent bond. For example, glucose and fructose combine to form the disaccharide sucrose (table sugar) (figure 2.12*a*).

Figure 2.12 **Carbohydrates**

(*a*) Glucose and fructose are monosaccharides that combine to form the disaccharide sucrose. (*b*) Glycogen is a polysaccharide formed by combining many glucose molecules. (*c*) Transmission electron micrograph of stored glycogen in a human cell. Glycogen clusters together into particles called granules.

(c) Biophoto Associates/Science Source

Polysaccharides (pol-ee-SACK-ah-rides; poly, many) consist of long chains of monosaccharides. Three important polysaccharides are: (1) glycogen, (2) starch, and (3) cellulose. **Glycogen,** or animal starch, is a polysaccharide of many glucose molecules (figure 2.12*b*). Glycogen is the main storage form of glucose in humans. Glucose is quickly broken down by cells to make ATP. Glycogen serves as a ready supply of more glucose for ATP production. **Starch** and **cellulose** are two important polysaccharides found in plants. Like glycogen, both are composed of long chains of glucose. Starch stores energy for plants in the same way as glucose stores energy for animals. Fortunately, when humans ingest starch, our cells can break it down and use the glucose to make ATP. However, humans cannot digest cellulose and it is eliminated in the feces, where it provides bulk. Clinically, the presence of cellulose (fiber) in our diet is important for regularity of bowel movements and has been reported to help reduce cholesterol and control blood sugar levels.

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Lipids

Lipids are a major group of organic molecules that are defined as being relatively insoluble in water. Lipids have many important functions in the body (table 2.4). They (1) provide protection and insulation, (2) help regulate many physiological processes, (3) form membranes, and (4) are major energy storage molecules, which can be broken down and used as an energy source. Like carbohydrates, lipids are composed mainly of carbon, hydrogen, and oxygen, but lipids have a lower ratio of oxygen to carbon than do carbohydrates. This makes them less polar.

The major classes of lipids are (1) fats, which are mostly triglycerides, (2) phospholipids, (3) eicosanoids, and (4) steroids. **Fats** are important energy-storage molecules; they also pad and insulate the body. The building blocks of fats are **glycerol** (GLIS-er-ol) and **fatty acids** (figure 2.13). Glycerol is a 3-carbon molecule with a **hydroxyl** (high-DROK-sil) **group** (—OH) attached to each carbon atom, and fatty acids consist of a carbon chain with a **carboxyl** (kar-BOK-sil) **group** attached at one end. A carboxyl group consists of both an oxygen atom and a hydroxyl group attached to a carbon atom (—COOH):

Figure 2.13 **Triglyceride**
One glycerol molecule and three fatty acids are combined to produce a triglyceride.

The carboxyl group is responsible for the acidic nature of the molecule because it releases H^+ into solution. **Triglycerides** (trie-GLISS-eh-rides) are the most common type of fat molecules and have three fatty acids bound to a glycerol molecule.

Fatty acids differ from one another according to the length and degree of saturation of their carbon chains. Most naturally occurring fatty acids contain 14 to 18 carbon atoms. A fatty acid is **saturated** if it contains only single covalent bonds between the carbon atoms (figure 2.14*a*). This means that each carbon is "full" with hydrogen, or saturated. Sources of saturated fats include beef, pork, whole milk, cheese, butter, eggs, coconut oil, and palm oil. The carbon chain is **unsaturated** if it has one or more double covalent bonds (figure 2.14*b*). The double covalent bonds introduce kinks into the carbon chain, which tends to keep them liquid at room temperature. **Monounsaturated fats,** such as olive and peanut oils, have one double covalent bond between carbon atoms. **Polyunsaturated fats,** such as safflower, sunflower, corn, and fish oils, have two or more double covalent bonds between carbon atoms. Unsaturated fats are the best type of fats in the diet because, unlike saturated fats, they do not contribute to the development of cardiovascular disease.

Figure 2.14 **Fatty Acids**

(*a*) Palmitic acid is a saturated fatty acid; it contains no double bonds between the carbons. (*b*) Linolenic acid is an unsaturated fatty acid; note the three double bonds between the carbons, which cause the molecule to have a bent shape.

***Trans* fats** are unsaturated fats that have been chemically altered by the addition of H atoms. The process makes the fats more saturated and hence more solid and stable (longer shelf-life). However, the change in structure of these chemicals makes the consumption of *trans* fats an even greater factor than saturated fats in the risk for cardiovascular disease.

Phospholipids are composed of a polar region containing phosphate and a nonpolar region consisting of two fatty acid chains (figure 2.15). The phosphate head of the phospholipid is said to be **hydrophilic** (water-loving), or **water-soluble.** The nonpolar end of a phospholipid is repelled by water and is said to be **hydrophobic** (water-fearing), or **lipid-soluble.** Phospholipids are important structural components of cell membranes (see chapter 3).

Figure 2.15 **Phospholipids**

(*a*) Molecular model of a phospholipid. Note that one of the fatty acid tails is bent, indicating that it is unsaturated. (*b*) A simplified depiction of a phospholipid.

The **eicosanoids** (EYE-koh-sah-noyds) are a group of important chemicals derived from fatty acids. Eicosanoids are made in most cells and are important regulatory molecules. Among their numerous effects is their role in the response of tissues to injuries. One example of eicosanoids is **prostaglandins** (PROS-tah-GLAN-dins), which have been implicated in regulating the secretion of some hormones, blood clotting, some reproductive functions, and many other processes. Many of the therapeutic effects of aspirin and other anti-inflammatory drugs result from their ability to inhibit prostaglandin synthesis.

Steroids are lipids that have four ringlike structures (figure 2.16). **Cholesterol** is an important steroid because other steroid molecules are synthesized from it. Steroids derived from cholesterol include bile salts (lipid digestion), estrogen, progesterone, and testosterone (reproductive hormones). In addition, cholesterol is an important component of cell membranes. Although high levels of cholesterol in the blood increase the risk of cardiovascular disease, a certain amount of cholesterol is vital for normal function.

Figure 2.16 **Steroids**

Steroids are four-ringed molecules that differ from one another according to the groups attached to the rings. Cholesterol, the most common steroid, can be modified to produce other steroids.

Proteins

Proteins have many important functions in the body (table 2.4): (1) regulation of body processes, (2) acting as a transportation system, (3) providing protection, (4) helping muscles contract, and (5) providing structure and energy. All proteins are organic macromolecules that contain carbon, hydrogen, oxygen, and nitrogen, bound together by covalent bonds. Most proteins also contain sulfur and some contain small amounts of phosphorus. The building blocks of proteins are **amino** (ah-MEE-noh) **acids,** which are organic acids containing an **amine** (ah-MEEN) **group** ($-NH_2$), a carboxyl group, and a side chain designated by the symbol **R** (figure 2.17*a*). There are 20 basic types of amino acids, which differ in their **R** group. Humans can synthesize 12 of them from simple organic molecules, but the remaining 8 so-called essential amino acids must be obtained in the diet.

Figure 2.17 **Protein Structure**

When a chain of amino acids is formed, chemical interactions between amino acids cause the entire chain to fold upon itself in predictable patterns.

A protein consists of many amino acids bound by covalent bonds called peptide bonds. The amino acids are placed in a specific sequence to form a chain (figure 2.17*b*,*c*). Although there are only around 20 different amino acids, they can combine to form numerous types of proteins with unique structures and functions. Similarly, the alphabet of the English language has only 26 letters, but more than 170,000 words can be formed from these. Different proteins have different kinds and numbers of

amino acids as dictated by different genes. Hydrogen bonds between amino acids in the chain cause the chain to fold or coil into a specific three-dimensional shape (figure 2.17*d*,*e*). The ability of proteins to perform their functions depends on their shape. If the hydrogen bonds that maintain the shape of the protein are broken, the protein becomes nonfunctional. This change in shape is called **denaturation,** and it can be caused by abnormally high temperatures or changes in pH.

Enzymes

Proteins perform many roles in the body, including acting as enzymes. Recall that enzymes increase the rate of chemical reactions without the enzyme being permanently changed. The three-dimensional shape of an enzyme is critical for its normal function. The shape of an enzyme and those of the reactants allow the enzyme to bind easily to the reactants. Bringing the reactants very close to one another reduces the activation energy for the reaction. Because the enzyme and the reactants must bind together, enzymes are very specific for the reactions they control. Each enzyme controls only one type of chemical reaction. After the reaction takes place, the enzyme is released unchanged and can be used again (figure 2.18).

Figure 2.18 **Enzyme Action**

The enzyme brings two reacting molecules together. This is possible because the reacting molecules "fit" the shape of the enzyme. After the reaction, the unaltered enzyme can be used again.

The body's chemical events are regulated primarily by mechanisms that control either the concentration or the activity of enzymes. Either (1) the rate at which enzymes are produced in cells or (2) whether the enzymes are in an active or inactive form determines the rate of each chemical reaction.

Nucleic Acids: DNA and RNA

The nucleic (noo-KLEE-ik) acids are large molecules composed of carbon, hydrogen, oxygen, nitrogen, and phosphorus. There are two types of nucleic acids: (1) **Deoxyribonucleic acid (**dee-OCK-see-RYE-boh-noo-KLEE-ik; **DNA**), which is the genetic material of cells. DNA contains genes, which determine the structure of proteins. (2) **Ribonucleic acid (**RYE-boh-noo-KLEE-ik; **RNA**), which is structurally related to DNA and important in protein synthesis. In chapter 3, we explore the means by which DNA and RNA direct the functions of the cell.

The basic building blocks of DNA and RNA are called **nucleotides** (NOO-klee-oh-tides). Nucleotides are composed of (1) a monosaccharide, (2) a nitrogenous base, and (3) a phosphate group (figure 2.19). The monosaccharide is deoxyribose for DNA, and ribose for RNA. The nitrogenous bases are thymine (THIGH-meen, THIGH-min), cytosine (SIGH-toh-seen), and uracil (YOOR-ah-sil), which are single-ringed molecules, and adenine (AD-eh-neen) and guanine (GWAHN-een), which are double-ringed molecules.

Figure 2.19 APR **Structure of DNA**

DNA is a double-helix molecule with two strands of nucleotides bound together by hydrogen bonds between adenine and thymine and between cytosine and guanine.

DNA has two strands of nucleotides joined together to form a twisted, ladderlike structure called a double helix. The sides of the ladder are formed by covalent bonds between the monosaccharides and phosphate groups of adjacent nucleotides. The rungs of the ladder are formed by the nitrogenous bases of the nucleotides of one side connected to the bases of the other side by hydrogen bonds. Each nucleotide of DNA contains one of the nitrogenous bases: adenine, thymine, cytosine, or guanine. Adenine binds only to thymine because the structure of these nitrogenous bases allows two hydrogen bonds to form between them. Cytosine binds only to guanine because the structure of these nitrogenous bases allows three hydrogen bonds to form between them.

The sequence of organic bases in DNA molecules stores information used to determine the structures and functions of cells. A sequence of DNA bases that directs the synthesis of proteins or RNA molecules is called a **gene** (see chapter 3, section 3.6, for more information on genes).

RNA has a structure similar to a single strand of DNA. Like DNA, four different nucleotides make up the RNA molecule, and the organic bases are the same, except that thymine is replaced with uracil. Uracil can bind only to adenine.

Adenosine Triphosphate

Adenosine triphosphate (ah-DEN-o-seen try-FOS-fate) **(ATP)** is the most important molecule for storing and providing energy in all living organisms. ATP consists of (1) adenosine (a monosaccharide with adenine) and (2) three phosphate groups (figure 2.20). The close proximity of the three negatively charged phosphate groups makes ATP a very unstable molecule. Breaking the phosphate bonds releases a large amount of energy; hence, the second and third phosphate bonds are referred to as "high-energy" bonds. In particular, the potential energy stored in the covalent bond between the second and third phosphate groups of ATP is important to living organisms because it provides the energy used in nearly all of the chemical reactions within cells. Removal of the third phosphate group generates **adenosine diphosphate (ADP),** which has only two phosphate groups and much less potential energy than ATP.

Figure 2.20 APR **Structure of ATP**

ATP releases energy when the bond between phosphate groups is broken. Notice that the bond between the oxygen atoms and phosphorus atoms of adjacent phosphate groups is drawn as a squiggly line. This symbolizes a less stable bond that is partly due to the negative charge on each phosphate and that, when broken, releases a great amount of energy. Consequently, this squiggly line is often referred to as a "high-energy" bond.

ATP is often called the energy currency of cells because it is capable of both storing and providing energy. The concentration of ATP is maintained within a narrow range of values, and essentially all energy-requiring chemical reactions stop when the

quantity of ATP becomes inadequate. For example, the poison cyanide is toxic because it interferes with the production of ATP by mitochondria (see chapter 3). The most common cause of cyanide poisoning is inhalation of smoke from burning rubber and plastic during a household fire. Cyanide gas was used to kill people during the Holocaust. Purposeful killing occurred when someone laced Tylenol with cyanide in 1982, leading to tamper-proof packaging of over-the-counter medicines.

SUMMARY

Chemistry is the study of the composition and structure of substances and the reactions they undergo.

2.1 Basic Chemistry

Matter, Mass, and Weight

1. Matter is anything that occupies space and has mass.
2. Mass is the amount of matter in an object, and weight results from the gravitational attraction between the earth and an object.

Elements and Atoms

1. An element is the simplest type of matter having unique chemical and physical properties.
2. An atom is the smallest particle of an element that has the chemical characteristics of that element. An element is composed of only one kind of atom.

Atomic Structure

1. Atoms consist of neutrons, positively charged protons, and negatively charged electrons.
2. An atom is electrically neutral because the number of protons equals the number of electrons.
3. Protons and neutrons are in the nucleus, and electrons can be represented by an electron cloud around the nucleus.
4. The atomic number is the unique number of protons in each atom of an element. The mass number is the number of protons and neutrons.
5. The chemical reactivity of an atom is determined by its electronegativity.
6. An atom that has closer to 8 electrons in its valence shell has a stronger electronegativity than an atom that has only 1 or 2 electrons in its valence shell.

Electrons and Chemical Bonding

1. An ionic bond results when an electron is transferred from an atom with a weaker electronegativity to an atom with a stronger electronegativity.
2. A covalent bond results when a pair of electrons is shared between atoms with similar electronegativities. A polar covalent bond is an unequal sharing of electron pairs.

Molecules and Compounds

1. A molecule is two or more atoms chemically combined to form a structure that behaves as an independent unit.
2. A compound is two or more different types of atoms chemically combined. A compound can be a molecule (covalent compound) or an organized array of ions (ionic compound).

Intermolecular Forces

A hydrogen bond is the weak attraction between the oppositely charged regions of polar molecules. Hydrogen bonds are important in determining the three-dimensional structure of large molecules.

Molecules and Compounds

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Dissociation

Dissociation is the separation of ions in an ionic compound by polar water molecules.

2.2 Chemical Reactions and Energy

Classification of Chemical Reactions

1. A synthesis reaction is the combination of reactants to form a new, larger product.
2. A decomposition reaction is the breakdown of larger reactants into smaller products.
3. An exchange reaction is a combination of a decomposition reaction, in which reactants are broken down, and a synthesis reaction, in which the products of the decomposition reaction recombine.
4. In a reversible reaction, the reactants can form products, or the products can form reactants.
5. The amount of reactant relative to the amount of product is constant at equilibrium.

Energy

1. Energy is the capacity to do work. Potential energy is stored energy that could do work, and kinetic energy does work by causing the movement of an object.

2. Energy exists in chemical bonds as potential energy.
3. Energy is released in chemical reactions when the products contain less potential energy than the reactants. The energy can be lost as heat, used to synthesize molecules, or used to do work.
4. Energy must be added in reactions when the products contain more potential energy than the reactants.
5. Energy can be neither created nor destroyed, but one type of energy can be changed into another.

Rate of Chemical Reactions

1. The rate of a chemical reaction increases when the temperature increases, or a catalyst is present.
2. A catalyst (enzyme) increases the rate of a chemical reaction without being altered permanently.

2.3 Acids and Bases

Acids are proton (H^+) donors, and bases are proton acceptors.

The pH Scale

1. A neutral solution has an equal number of H^+ and OH^- and a pH of 7.0.
2. An acidic solution has more H^+ than OH^- and a pH less than 7.0.
3. A basic solution has fewer H^+ than OH^- and a pH greater than 7.0.

Salts

A salt forms when an acid reacts with a base.

Buffers

Buffers are chemicals that resist changes in pH when acids or bases are added.

2.4 Inorganic Molecules

1. Inorganic chemistry is mostly concerned with non-carbon-containing substances but does include such carbon-containing substances as CO_2 and carbon monoxide.
2. Some inorganic chemicals play important roles in the body.

Oxygen and Carbon Dioxide

1. Oxygen is involved with the extraction of energy from food molecules.
2. Carbon dioxide is a by-product of the breakdown of food molecules.

Water

1. Water stabilizes body temperature.
2. Water provides protection by acting as a lubricant or a cushion.
3. Water is necessary for many chemical reactions.

2.5 Organic Molecules

Organic molecules contain carbon atoms bound together by covalent bonds.

Carbohydrates

1. Carbohydrates provide the body with energy.
2. Monosaccharides are the building blocks that form more complex carbohydrates, such as disaccharides and polysaccharides.

Lipids

1. Lipids are organic molecules that dissolve in nonpolar solvents, such as alcohol or acetone, but not in polar solvents, such as water. Fats, phospholipids, and steroids are examples of lipids.
2. Lipids provide energy (fats), serve as structural components (phospholipids), and regulate physiological processes (steroids).
3. The building blocks of triglycerides (fats) are glycerol and fatty acids.
4. Fatty acids can be saturated (have only single covalent bonds between carbon atoms) or unsaturated (have one or more double covalent bonds between carbon atoms).

Proteins

1. Proteins regulate chemical reactions (enzymes), serve as structural components, and cause muscle contraction.
2. The building blocks of proteins are amino acids.
3. Denaturation of proteins disrupts hydrogen bonds, which changes the shape of proteins and makes them nonfunctional.
4. Enzymes are specific, bind to reactants according to the lock-and-key model, and function by lowering activation energy.

Nucleic Acids: DNA and RNA

1. The basic unit of nucleic acids is the nucleotide, which is a monosaccharide with an attached phosphate and nitrogenous base.
2. DNA nucleotides contain the monosaccharide deoxyribose and the organic bases adenine, thymine, guanine, and cytosine. DNA occurs as a double strand of joined nucleotides and is the genetic material of cells.

3. RNA nucleotides are composed of the monosaccharide ribose. The organic bases are the same as for DNA, except that thymine is replaced with uracil.

Adenosine Triphosphate

ATP stores energy, which can be used in cell processes.

REMEMBERING AND UNDERSTANDING

1. Define chemistry. Why is an understanding of chemistry important to the study of human anatomy and physiology?
2. Define matter. What is the difference between mass and weight?
3. Define element and atom. How many different kinds of atoms are present in a specific element?
4. List the components of an atom, and explain how they are organized to form an atom. Compare the charges of the subatomic particles.
5. Define the atomic number and the mass number of an element.
6. Distinguish among ionic, covalent, polar covalent, and hydrogen bonds. Define ion.
7. What is the difference between a molecule and a compound?
8. What happens to ionic and covalent compounds when they dissolve in water?
9. Define chemical reaction. Describe synthesis, decomposition, and exchange reactions, giving an example of each.
10. What is meant by the equilibrium condition in a reversible reaction?
11. Define potential energy and kinetic energy.
12. Give an example of a chemical reaction that releases energy and an example of a chemical reaction that requires the input of energy.
13. Name two ways the rate of chemical reactions can be increased.
14. What is an acid and what is a base? Describe the pH scale.
15. Define a salt. What is a buffer, and why are buffers important?
16. Distinguish between inorganic and organic chemistry.
17. Why is O_2 necessary for human life? Where does the CO_2 we breathe out come from?
18. List three functions that water performs in the human body.

19. Name the four major types of organic molecules. Give a function for each.
20. Describe the action of enzymes in terms of activation energy and the lock-and-key model.

CRITICAL THINKING

1. Potassium (K) has 19 protons in its nucleus, whereas chlorine (Cl) has 17 protons. Explain which type of bond K and Cl will form. Give your reasoning.
2. For each of the following chemical equations, determine if a synthesis reaction, a decomposition reaction, or dissociation has taken place:

   a. $$\mathrm{HCl} \rightarrow \mathrm{H}^{+} + \mathrm{Cl}^{-}$$

   b. $$\text{Glucose} + \text{Fructose} \rightarrow \text{Sucrose (table sugar)}$$

   c. $$2\mathrm{H_2O} \rightarrow 2\mathrm{H_2} + \mathrm{O_2}$$

3. In terms of the energy in chemical bonds, explain why eating food is necessary for increasing muscle mass.
4. Given that the H^+ concentration in a solution is based on the following reversible reaction,

   $$\mathrm{CO_2} + \mathrm{H_2O} \rightleftarrows \mathrm{H}^{+} + \mathrm{HCO_3}^{-}$$

   what happens to the pH of the solution when $NaHCO_3$ (sodium bicarbonate) is added to the solution? (*Hint:* The sodium bicarbonate dissociates to form Na^+ and HCO_3^-.)
5. A mixture of chemicals is warmed slightly. As a consequence, although little heat is added, the solution becomes very hot. Explain what happens to make the solution hot.
6. Two solutions, when mixed together at room temperature, produce a chemical reaction. However, when the solutions are boiled and allowed to cool to room temperature before mixing, no chemical reaction takes place. Explain.

Answers to this chapter's odd-numbered Critical Thinking questions are in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

3

Cell Structures and Their Functions

The cell is the basic unit of life and is composed of a cell membrane and the cytoplasm, which includes organelles such as the nucleus.

LEARN TO APPLY IT

Carlos has diabetes insipidus, an incurable disease that causes his kidneys to produce an unusually large volume of dilute urine. He always carries a water bottle, and he never likes to be too far from a restroom. To keep his body fluids in a state of homeostasis (see chapter 1), Carlos has to drink enough water to replace what he loses as urine. Diabetes insipidus is a genetic disease in which the body does not respond normally to an important chemical signal called ADH, which regulates water loss at the kidneys.

After reading about cell structure and genetic expression in chapter 3, explain how Carlos's condition developed at the cellular level.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 2 Cells and Chemistry

3.1 CELL STRUCTURE

Learning Outcome *After reading this section, you should be able to*

A. Explain how the structures of a cell contribute to its function.

The study of cells is an important link between the study of chemistry in chapter 2 and the study of tissues in chapter 4. Knowledge of chemistry makes it possible to understand cells because cells are composed of chemicals, and those chemicals are responsible for the cells' characteristics.

Cells, in turn, determine the form and functions of the human body. From cellular function, we can progress to the study of tissues. In addition, many human diseases and other disorders have a cellular basis. The human body is composed of trillions of cells and acts as a host to countless other organisms (see "Microbes In Your Body: Getting to Know Your Bacteria" in chapter 1). Because the body is made of many, many cells, we must first understand the anatomy and physiology of the cell before we can understand the anatomy and physiology of the human body.

The cell is the basic living unit of all organisms. The simplest organisms consist of single cells, whereas humans are composed of multiple cells. An average-sized cell is one-fifth the size of the smallest dot you can make on a sheet of paper with a sharp pencil! But despite their extremely small size, cells are complex living structures. Cells have many characteristics in common; however, most cells are also specialized to perform specific functions. The human body is made up of many populations of specialized cells. The coordinated functions of these populations are critical to the survival of humans and all other complex organisms. This chapter considers the structures of cells and how cells perform the activities necessary for maintaining homeostasis.

Each cell is a highly organized unit. Within cells, specialized structures called **organelles** (OR-gah-nellz; little organs) perform specific functions

(figure 3.1 and table 3.1). The nucleus is an organelle containing the cell's genetic material. The living material surrounding the nucleus is called **cytoplasm** (SIGH-toh-plazm), and it contains many types of organelles. The cytoplasm is enclosed by the **cell membrane,** or *plasma membrane.*

TABLE 3.1 Organelles and Their Locations and Functions

Organelles	Location	Function(s)
Nucleus	Variable location within cell	Contains genetic material of cell (DNA) and nucleoli; site of RNA synthesis and ribosomalsubunit assembly
Ribosomes	In cytoplasm	Site of protein synthesis
Rough endoplasmic reticulum (rough ER)	In cytoplasm	Has many ribosomes attached; site of protein synthesis
Smooth endoplasmic reticulum (smooth ER)	In cytoplasm	Site of lipid synthesis; participates in detoxification
Golgi apparatus	In cytoplasm	Modifies protein structure and packages proteins in secretory vesicles
Secretory vesicle	In cytoplasm	Contains materials produced in the cell; formed by the Golgi apparatus; secreted by exocytosis
Lysosome	In cytoplasm	Contains enzymes that digest material taken into the cell; formed by the Golgi apparatus
Peroxisome	In cytoplasm	Breaks down fatty acids, amino acids, and hydrogen peroxide
Mitochondrion	In cytoplasm	Site of aerobic respiration and the major site of ATP synthesis
Microtubule	In cytoplasm	Supports cytoplasm; assists in cell division and forms components of cilia and flagella
Centrioles	In cytoplasm	Facilitate the movement of chromosomes during cell division
Cilia	On cell surface with many on each cell	Move substances over surfaces of certain cells
Flagella	On sperm cell surface with one per cell	Propel sperm cells

Organelles	Location	Function(s)
Microvilli	Extensions of cell surface with many on each cell	Increase surface area of certain cells

The number and type of organelles within each cell determine the cell's specific structure and functions. For example, cells secreting large amounts of protein contain well-developed organelles that synthesize and secrete protein, whereas muscle cells contain proteins and organelles that enable them to contract. The following sections describe the structure and main functions of the major components of cells.

3.2 FUNCTIONS OF THE CELL

Learning Outcome *After reading this section, you should be able to*

A. List the four main functions of a cell.

Cells are commonly defined as "the smallest units of life," meaning they have all the characteristics of life, as described in chapter 1. Though the cells of the human body are very diverse, most share common functions. The following are four important functions performed by our body cells:

1. *Cell metabolism and energy use.* The chemical reactions that occur within cells are collectively called **cell metabolism.** Energy released during metabolism is used for cell activities, such as the synthesis of new molecules, muscle contraction, and heat production, which helps maintain body temperature.
2. *Synthesis of molecules.* Cells synthesize various types of molecules, including proteins, nucleic acids, and lipids. The different cells of the body do not all produce the same molecules. Therefore, a cell's structural and functional characteristics are determined by the types of molecules the cell produces.
3. *Communication.* Cells produce and receive chemical and electrical signals that allow them to communicate with one another. For example, nerve cells communicate with one another and with muscle cells, causing muscle cells to contract.
4. *Reproduction and inheritance.* Each cell contains a copy of the genetic information of the individual. Specialized cells (sperm cells and oocytes) transmit that genetic information to the next generation.

3.3 CELL MEMBRANE

Learning Outcome *After reading this section, you should be able to*

A. Describe the structure of the cell membrane.

The **cell membrane,** or *plasma* (PLAZ-mah) *membrane,* is the outermost component of a cell. The cell membrane encloses the cytoplasm and forms the boundary between material inside the cell and material outside it. Substances outside the cell are called **extracellular** substances, and those inside the cell are called **cytoplasmic,** or *intracellular,* substances. Besides enclosing the cell, the cell membrane has other functions, including (1) supporting the cell contents, (2) acting as a selective barrier that determines what moves into and out of the cell, and (3) playing a role in communication between cells. The cell membrane is primarily made up of two major types of molecules: (1) phospholipids and (2) proteins. In addition, the membrane contains other molecules, such as (3) cholesterol and (4) carbohydrates.

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Studies of the arrangement of molecules in the cell membrane have given rise to a model of its structure called the **fluid-mosaic model** (figure 3.2). The phospholipids form a double layer of molecules. The polar, phosphate-containing ends of the phospholipids are hydrophilic (water-loving) and therefore face the extracellular fluid and cytoplasm of the cell. The nonpolar, fatty acid ends of the phospholipids are hydrophobic (water-fearing) and therefore face away from the fluid on either side of the membrane, toward the center of the double layer of phospholipids. The double layer of phospholipids forms a lipid barrier between the inside and outside of the cell. Take a moment and draw your own representation of a phospholipid bilayer, paying attention to the position of the phospholipid molecules as described above. Compare your drawing to figure 3.2.

Figure 3.2 APR **Cell Membrane**

(*a*) Fluid-mosaic model of the cell membrane. The membrane is composed of a bilayer of phospholipids and cholesterol with proteins "floating" in the membrane. The nonpolar hydrophobic region of each phospholipid molecule is directed toward the center of the membrane, and the polar hydrophilic region is directed toward the fluid environment either outside or inside the cell. (*b*) Colorized transmission electron micrograph showing the cell membrane of a single cell. Proteins at either surface of the lipid bilayer stain more readily than the lipid bilayer does and give the membrane the appearance of having three parts: The two yellow, outer parts are proteins and the phospholipid heads, and the blue, central part is the phospholipid tails and cholesterol.

(b) Don W. Fawcett/Science Source

The double layer of phospholipids has a fluid quality, meaning that the phospholipids are not completely stationary but are able to move. Cholesterol within the phospholipid membrane gives it added strength and stability by limiting how much the phospholipids can move. Protein molecules "float" among the phospholipid molecules and, in some cases, extend from the inner to the outer surface of the cell membrane. Carbohydrates may be bound to some protein molecules, modifying their functions. The membrane proteins function as membrane channels, carrier molecules, receptor molecules, enzymes, or structural supports in the membrane. Membrane channels and carrier molecules are involved with the movement of substances through the cell membrane. Receptor molecules are part of an intercellular communication system that enables cell recognition and coordination of the activities of cells. For example, a nerve cell can release a chemical messenger that moves to a muscle cell and temporarily binds to a receptor on the muscle

cell membrane. The binding acts as a signal that triggers a response, such as contraction of the muscle cell.

3.4 MOVEMENT THROUGH THE CELL MEMBRANE

Learning Outcomes ***After reading this section, you should be able to***

- **A.** Define diffusion and concentration gradient.
- **B.** Explain the role of osmosis and that of osmotic pressure in controlling the movement of water across the cell membrane.
- **C.** Compare hypotonic, isotonic, and hypertonic solutions and describe how each of these solutions affects the shape of a cell.
- **D.** Define carrier-mediated transport.
- **E.** Compare and contrast the processes of facilitated diffusion, active transport, and secondary active transport.
- **F.** Describe endocytosis and exocytosis.

Cell membranes are **selectively permeable,** meaning that they allow some substances, but not others, to pass into or out of the cells. Cytoplasmic material has a different composition than extracellular material, and the cell's survival depends on maintaining the difference. Substances such as enzymes, glycogen, and potassium ions (K^+) are found in greater concentrations inside the cell, whereas Na^+, Ca^{2+}, and Cl^- are found in greater concentrations in the extracellular fluid. In addition, nutrients must enter cells continually, and waste products must exit. Because of the permeability characteristics of cell membranes and their ability to transport certain molecules, cells are able to maintain proper cytoplasmic concentrations of molecules. Rupture of the membrane, alteration of its permeability characteristics, or inhibition of transport processes can disrupt the normal cytoplasmic concentration of molecules and lead to cell death.

Protein
Phospholipid
Chromatin
Nuclear envelope
Nucleolus
Nuclear pore
Nucleoplasm
Nucleus
Cell membrane
Cytoplasm
Centrioles
Centrosome
Ribosome
Rough endoplasmic reticulum
Smooth endoplasmic reticulum
Free ribosome

Cilia
Secretory vesicles
Microvilli
Golgi apparatus
Mitochondrion
Peroxisome

Figure 3.1 APR **Generalized Cell**

This generalized cell shows the major organelles contained in cells. However, no single cell contains all of these organelle types. Furthermore, one kind of cell may contain many organelles of one type, whereas another kind of cell may contain very few.

Passive Membrane Transport

Movement through the cell membrane may be passive or active. Passive membrane transport does not require the cell to expend energy. Active membrane transport does require the cell to expend energy, usually in the form of ATP. Passive membrane transport mechanisms include (1) diffusion, (2) osmosis, and (3) facilitated diffusion. Active membrane transport mechanisms include (1) active transport, (2) secondary active transport, (3) endocytosis, and (4) exocytosis. Table 3.2 lists the specific types of movement across cell membranes and we discuss each method in detail in the following sections.

TABLE 3.2 Types and Characteristics of Movement Across Membranes

Types	Transport	Requires ATP	Examples
Passive Membrane Transport			

Types	Transport	Requires ATP	Examples
Diffusion	With the concentration gradient through the lipid portion of the cell membrane or through membrane channels	No	O_2, CO_2, Cl^-, urea
Osmosis	With the concentration gradient (for water) through the lipid portion of the cell membrane or through membrane channels	No	Water
Facilitated diffusion	With the concentration gradient by carrier molecules	No	Glucose in most cells
Active Membrane Transport			
Active transport	Against the concentration gradient* by carrier molecules	Yes	Na^+, K^+, Ca^{2+}, H^+, and amino acids
Secondary active transport	Against the concentration gradient by carrier molecules; the energy for secondary active transport of one substance comes from the concentration gradient of another	Yes	Glucose, amino acids
Endocytosis	Movement into cells by vesicles	Yes	Ingestion of particles by phagocytosis or receptor-mediated endocytosis and liquids by pinocytosis
Exocytosis	Movement out of cells by vesicles	Yes	Secretion of proteins
*Active transport normally moves substances against their concentration gradient, but it can also move substances with their concentration gradient.			

Diffusion

Both cytoplasm and extracellular fluid are solutions. A **solution** is generally composed of two major parts, solutes and the solvent. **Solutes** are substances dissolved in a predominant liquid or gas, which is called the **solvent.** Solutes, such as ions or molecules, are in constant motion. Each solute tends to move from an area where it is in higher concentration to an area where it is in lower concentration in solution. This process is called **diffusion.** An example of diffusion is the distribution of smoke throughout a room in which there are no air currents. Another example of diffusion is the gradual spread of salt throughout a beaker of still water, which is illustrated in figure 3.3.

PROCESS Figure

PROCESS Figure 3.3 APR **Diffusion**

Illustration of diffusion of a salt (small dots) in a beaker of water.

Apply **How would changing the temperature of the solution affect the diffusion of the salt crystals?**

1. When a salt crystal is placed into a beaker of water, a concentration gradient exists between the salt from the salt crystal and the water that surrounds it.
2. Salt ions move down their concentration gradient into the water.
3. Salt ions and water molecules are distributed evenly throughout the solution.

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Diffusion results from the natural, constant random motion of all solutes in a solution. More solute particles occur in an area of higher concentration than in an area of lower concentration. Because particles move randomly, the chances are greater that solute particles will move from the higher toward the lower concentration than from the lower toward the higher concentration. At equilibrium, the net movement of solutes stops, although the random motion

continues, and the movement of solutes in any one direction is balanced by an equal movement of solutes in the opposite direction (figure 3.3, step 3).

A **concentration gradient** is the difference in the concentration of a solute in a solvent between two points divided by the distance between the two points. The concentration gradient is said to be steeper when the concentration difference is large and/or the distance is small. When we say that a substance moves down (or with) its concentration gradient, we mean that the solute is diffusing from an area of higher concentration toward an area of lower concentration of that specific solute. When we say that a solute moves up (or against) its concentration gradient, this means that the substance moves from an area of lower solute concentration to an area of higher solute concentration. Note that this second type of movement (movement up a concentration gradient) does not occur by diffusion and requires energy.

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In the body, diffusion is an important means of transporting substances through the extracellular fluid and cytoplasm. In addition, substances, such as nutrients and some waste products, can diffuse into and out of the cell. The normal cytoplasmic concentrations of many substances depend on diffusion. For example, if the extracellular concentration of O_2 is reduced, not enough O_2 diffuses into the cell, and the cell cannot function normally.

Apply It 1

Urea is a toxic waste produced inside liver cells. It diffuses from those cells into the blood and is eliminated from the body by the kidneys. What would happen to the cytoplasmic and extracellular concentrations of urea if the kidneys stopped functioning?

Osmosis

The solvent of a solution is also composed of molecules that are in constant random motion. As such, solvent molecules are subject to diffusion as well. When water is the solvent of a solution, we use a specific term to refer to its movement. **Osmosis** (oz-MOH-sis) is the diffusion of water across a selectively permeable membrane, such as the cell membrane, from a region of higher water concentration to one of lower water concentration (figure 3.4; see table 3.2). Even though water is a polar molecule, it is small enough that it can move across the cell membrane by passing either between the

phospholipid molecules or through water channels. Osmosis is important to cells because large volume changes caused by water movement can disrupt normal cell functions. Osmosis occurs when the cell membrane is less permeable, selectively permeable, or not permeable to solutes *and* a concentration gradient for water exists across the cell membrane. Water diffuses from a solution with a higher water concentration across the cell membrane into a solution with a lower water concentration. The ability to predict the direction of water movement across the cell membrane depends on knowing which solution on either side of the membrane has the higher water concentration.

PROCESS Figure

PROCESS Figure 3.4 APR Osmosis

Water moves from the beaker across the selectively permeable membrane into a tube containing a solution with a higher salt concentration.

Apply

Addison disease results from a decrease in secretion of aldosterone, a hormone that allows kidney cells to transport Na^+ from the urine back into the blood. How would this affect the Na^+ in the urine? Would you expect urine volume to be higher or lower than normal? Explain your answer.

The concentration of a solution, however, is expressed not in terms of water, but in terms of solute concentration. For example, if sugar solution A is more concentrated than sugar solution B, then solution A has more sugar (solute) than solution B. As the concentration of a solution increases, the amount of water (solvent) proportionately decreases. Water diffuses from the less concentrated solution B (less sugar, more water), into the more concentrated solution A (more sugar, less water). In other words, water diffuses toward areas of high solute concentration and dilutes those solutes. An easy way to remember the direction of water movement is "water follows solutes." Water moves to the area with the greater solute concentration.

Osmotic pressure is the force required to prevent the movement of water across a selectively permeable membrane. Thus, osmotic pressure is a measure of the tendency of water to move by osmosis across a selectively permeable membrane. Figure 3.4 illustrates the process of osmosis across a selectively permeable membrane, as well as the concept of osmotic pressure.

❶ Osmotic pressure can be measured by placing a solution into a tube that is closed at one end by a selectively permeable membrane and immersing the tube in distilled water.

❷ Water molecules move by osmosis through the membrane into the tube, forcing the solution to move up the tube.

❸ As the solution rises, the weight of the solution produces **hydrostatic pressure,** which pushes water out of the tube back into the distilled water surrounding the tube. Net movement of water into the tube stops when the hydrostatic pressure in the tube causes water to move out of the tube at the same rate at which it diffuses into the tube by osmosis. The osmotic pressure of the solution in the tube is equal to the hydrostatic pressure that prevents net movement of water into the tube.

The greater the concentration of a solution, the greater its osmotic pressure, and the greater the tendency for water to move into the solution. This occurs because water moves from less concentrated solutions (less solute, more water) into more concentrated solutions (more solute, less water). The greater the concentration of a solution, the greater the tendency for water to move into the solution, and the greater the osmotic pressure must be to prevent that movement from occurring.

When placed into a solution, a cell may swell, remain unchanged, or shrink, depending on the concentration gradient between the solution and the cell's cytoplasm. A **hypotonic** (hye-poh-TON-ik (figure 3.5*a*). When a cell is immersed in an **isotonic** (EYE-soh-TON-ik; *iso,* equal) solution, the concentrations of various solutes and water are the same on both sides of the cell membrane. The cell therefore neither shrinks nor swells (figure 3.5*b*). A

hypertonic (hye-per-TON-ik; *hyper,* above) solution has a higher concentration of solutes and a lower concentration of water relative to the cytoplasm of the cell. When a cell is immersed in a hypertonic solution, water moves by osmosis from the cell into the hypertonic solution, resulting in cell shrinkage, or **crenation** (kreh-NAY-shun or kree-NAY-shun) (figure 3.5*c*). In general, solutions injected into blood vessels or into tissues must be isotonic to the body's cells because swelling or shrinking disrupts normal cell function and can lead to cell death.

Figure 3.5 **Effects of Hypotonic, Isotonic, and Hypertonic Solutions on Red Blood Cells**
The shape of a cell may change when it is placed in a new solution.
David M. Phillips/Science Source

Facilitated Diffusion

Though most lipid-soluble molecules, such as O_2, CO_2, and steroids, pass easily through the phospholipid bilayer, that is not the case with all molecules. The phospholipid bilayer acts as a barrier to most water-soluble substances, though certain small, water-soluble substances can diffuse between the phospholipid molecules of cell membranes. Other water-soluble substances, such as ions, diffuse across the cell membrane by passing through cell membrane **channels** (figure 3.6) or through **carrier molecules.**

Facilitated diffusion is a mediated transport process, involving membrane proteins such as channels or carrier proteins, to move substance across the cell membrane. As is the case with any type of diffusion, facilitated diffusion involves the movement of substances from an area of higher concentration to an area of lower concentration (see table 3.2). Facilitated diffusion is necessary due to the selectively permeable nature of the membrane.

Figure 3.6 **Diffusion Through the Cell Membrane**

Non-lipid-soluble molecules (*small red*) diffuse through membrane channels. Lipid-soluble molecules (*orange*) diffuse directly through the cell membrane.

Cell membrane channels consist of large protein molecules that extend from one surface of cell membranes to the other (figure 3.7). There are several channel types, each of which allows only certain substances to pass through. Characteristics of an ion or molecule determine whether it can pass through a channel. These characteristics include (1) size, (2) shape, and (3) charge. For example, Na^+ passes through Na^+ channels, and K^+ pass through K^+ channels. Rapid movement of water across the cell membrane also occurs through membrane channels. Consider how this information is relevant to the Learn to Apply It question at the beginning of the chapter.

Figure 3.7 **Leak and Gated Membrane Channels**

In this example, the K^+ leak channel (*purple*) is always open, allowing K^+ to diffuse across the cell membrane. The gated Na^+ channel (*pink*) regulates the movement of Na^+ across the membrane by opening and closing.

Cell membrane channels vary in structure and therefore also vary in the degree to which ions pass through them. Two classes of cell membrane channels include leak channels and gated channels. **Leak channels** constantly allow ions to pass through. **Gated channels** limit the movement of ions across the membrane by opening and closing (figure 3.7).

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Carrier molecules, which are proteins within the cell membrane, are also involved in facilitated diffusion. Carrier molecules can move water-soluble molecules or electrically charged ions across the cell membrane, as seen in figure 3.8.

PROCESS Figure

PROCESS Figure 3.8 APR **Facilitated Diffusion**

A carrier molecule transports glucose across the cell membrane from an area of higher glucose concentration (outside the cell) to an area of lower glucose concentration (inside the cell).

Explain why the carrier molecule represented in this figure would not likely transport amino acids across the cell membrane.

❶ A molecule to be transported binds to a specific carrier molecule on one side of the membrane.

❷ The binding of the molecule to the carrier molecule in the cell membrane causes the three-dimensional shape of the carrier molecule to change, and the transported molecule is moved to the opposite side of the cell membrane. The transported molecule is then released by the carrier molecule, which resumes its original shape and is available to transport another molecule.

Similar to channels, carrier molecules exhibit **specificity;** that is, only specific molecules are transported by the carriers. Carrier molecules are

commonly identified by the specific substance they transport. For example, glucose carrier molecules move glucose across the membrane.

Apply It 2

The transport of glucose into most cells occurs by facilitated diffusion. Because diffusion occurs from a higher to a lower concentration, glucose cannot accumulate within these cells at a higher concentration than exists outside the cell. Once glucose enters a cell, it is rapidly converted to other molecules, such as glucose phosphate or glycogen. What effect does this conversion have on the cell's ability to transport glucose?

Active Membrane Transport

Active Transport

Active transport is a process that utilizes membrane proteins to move substances across the cell membrane from regions of lower concentration to those of higher concentration, against a concentration gradient (see table 3.2). Consequently, active transport processes accumulate substances on one side of the cell membrane at concentrations many times greater than those on the other side. These dramatic concentration differences are important for normal cell activity. Active transport requires energy in the form of ATP; if ATP is not available, active transport stops. One example of active transport is the movement of various amino acids from the small intestine into the blood. The malfunction of active transport can lead to serious health conditions. **Cystic fibrosis** is a genetic disorder that affects the active transport of Cl^- into cells. This disorder is described in the Clinical Impact essay later in this chapter.

In some cases, the active transport mechanism can exchange one substance for another. For example, the **sodium-potassium pump** moves Na^+ out of cells and K^+ into cells (figure 3.9). The result is a higher concentration of Na^+ outside the cell and a higher concentration of K^+ inside the cell. The concentration gradients for Na^+ and K^+, established by the sodium-potassium pump, are essential in maintaining the resting membrane potential (see chapter 8).

Figure 3.9 **Active Transport: Sodium-Potassium Pump**
The sodium-potassium pump requires ATP to move Na^+ out of the cell and K^+ into the cell.

Secondary Active Transport

Secondary active transport involves the active transport of one substance, such as Na^+, across the cell membrane, establishing a concentration gradient, which then provides the energy for moving a second substances across the membrane. Figure 3.10 illustrates secondary active transport of glucose using a Na^+ concentration gradient.

PROCESS Figure

PROCESS Figure 3.10 **Secondary Active Transport**
The active transport of Na^+ out of the cell (step 1) maintains a Na^+ concentration gradient, which provides the energy for moving glucose against its concentration gradient (step 2).

Understand **In which step is the cell "paying" the energy cost for the transport of glucose against its concentration gradient? Explain your answer.**

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CLINICAL IMPACT

Cystic Fibrosis

Cystic fibrosis is a genetic disorder that occurs at a rate of approximately 1 per 2000 births and currently affects 33,000 people in the United States. It is the most common lethal genetic disorder among white individuals. The diagnosis is based on the following signs: recurrent respiratory disease, increased Na^+ in the sweat, and high levels of unabsorbed fats in the stool. Approximately 98% of all cases of cystic fibrosis are diagnosed before the patient is 18 years old.

At the molecular level, cystic fibrosis results from an abnormality in Cl^- channels. Normally, as Cl^- moves out of cells that line body tubes, such as ducts or respiratory passages, water follows by osmosis. In cystic fibrosis, Cl^- does not exit these cells at normal rates, and therefore less water moves into the tubes. With less water present, the mucus secreted by the cells lining those tubes is thick, and the cells' cilia cannot readily move the mucus over the cell surface. As a result, the tubes become clogged with mucus and lose much of their normal function.

The most critical effects of cystic fibrosis, accounting for 90% of deaths, are on the respiratory system.

In normal lungs, ciliated cells move a thin, fluid layer of mucus. In people with cystic fibrosis, the viscous mucus resists movement by cilia and accumulates in the lung passages. The accumulated mucus obstructs the passageways and increases the likelihood of infections. Infections are frequent and may result in chronic pneumonia. Chronic coughing occurs as the affected person attempts to remove the mucus.

At one time, cystic fibrosis was fatal during early childhood, but many patients are now surviving into young adulthood because of modern medical treatment. Currently, approximately 80% of people with cystic fibrosis live past age 20. Pulmonary therapy consists of supporting and enhancing existing respiratory functions, including drugs that are prescribed based on specific gene mutations. In addition, infections are treated with antibiotics.

Cystic fibrosis also affects the secretory cells lining the ducts of the pancreas, sweat glands, and salivary glands. The buildup of thick mucus in the pancreatic and hepatic ducts blocks them so that pancreatic digestive enzymes and bile salts cannot reach the small intestine. As a result, normal digestive functions are hindered and the patient

suffers from vitamin deficiencies which result in conditions such as night blindness, skin disorders, rickets, and excessive bleeding. Therapy includes supplementing pancreatic enzymes and administering the missing vitamins to the patient as well as dietary changes.

Apply It 3

Predict the effect of cystic fibrosis on the concentrations of Cl^- inside and outside the cell.

❶ A Na^+-K^+ pump actively moves Na^+ out of the cell, maintaining a higher concentration of Na^+ outside of the cell compared to the cytoplasm.

❷ The diffusion of Na^+ down its concentration gradient provides the energy to transport a second substance, in this example glucose, across the cell membrane.

In **cotransport,** the diffusing substance moves in the same direction as the transported substance; in **countertransport,** the diffusing substance moves in a direction opposite to that of the transported substance.

Endocytosis and Exocytosis

Large water-soluble molecules that cannot be transported by carrier molecules, small pieces of matter, and even whole cells can be transported across cell membranes in membrane-bound sacs called **vesicles** (VES-ih-kull; a bladder). Because of the fluid nature of membranes, vesicles and cell membranes can fuse, allowing the contents of the vesicles to cross the cell membrane.

Endocytosis (EN-doh-sigh-TOH-sis) is the uptake of material through the cell membrane by the formation of a vesicle (see table 3.2). The cell membrane invaginates (folds inward) to form a vesicle containing the material to be taken into the cell. The vesicle then moves into the cytoplasm.

Endocytosis usually exhibits specificity, through the process of **receptor-mediated endocytosis.** Figure 3.11 illustrates this type of membrane transport.

PROCESS Figure

PROCESS Figure 3.11 **Receptor-Mediated Endocytosis**

Molecules bind to receptors on the cell membrane, and a vesicle forms to transport the molecules into the cell.

What characteristic of the receptors allows the cell to control which molecules are transported into the cell?

❶ The cell membrane contains specific receptor molecules that bind to certain molecules.

❷ When the specific molecules bind to the receptors, endocytosis is triggered. A vesicle begins to form, bringing the receptors and the bound molecules into the cell.

❸ The vesicle forms completely in the cytoplasm as its membrane separates from the cell membrane.

Cholesterol and growth factors are examples of molecules that can be taken into a cell by receptor-mediated endocytosis. Endocytosis of bacterial cells is

also receptor-mediated.

The term **phagocytosis** (FAG-oh-sigh-TOH-sis; cell-eating) is often used for endocytosis when solid particles are ingested. A part of the cell membrane extends around a particle and fuses so that the particle is surrounded by the membrane. That part of the membrane then “pinches off” to form a vesicle containing the particle. The vesicle is now within the cytoplasm of the cell, and the cell membrane is left intact. White blood cells and some other cell types phagocytize bacteria, cell debris (fragments of dead cells), and foreign particles. Phagocytosis is an important means by which white blood cells take up and destroy harmful substances that have entered the body. **Pinocytosis** (PIN-oh-sigh-TOH-sis; cell-drinking) is distinguished from phagocytosis in that much smaller vesicles are formed, and they contain liquid rather than solid particles.

Exocytosis (EK-so-sy-TOH-sis; *exo* outside) is the release of substances from the cell through the fusion of a vesicle with the cell membrane (see table 3.2). Figure 3.12 illustrates exocytosis.

PROCESS Figure

PROCESS Figure 3.12 **Exocytosis**

(*a*) Diagram of exocytosis. (*b*) Transmission electron micrograph of exocytosis.

(b) ©Dr. Birgit H. Satir

Understand **What is the benefit of exocytosis versus the movement of substance out of the cell by the use of carrier molecules?**

❶ A membrane-bound sac called a **secretory vesicle** accumulates materials for release from the cell.

❷ The secretory vesicle moves to the cell membrane, where the vesicle membrane fuses with the cell membrane.

❸ The material in the vesicle is released from the cell. Examples of exocytosis are the secretion of digestive enzymes by the pancreas and the secretion of mucus by the salivary glands.

Endocytosis results in the uptake of materials by cells, and exocytosis allows for the release of materials from cells. In some cases, such as endothelial cells of blood capillaries, material is moved through the cell by the process of **transcytosis.** During transcytosis, a substance is taken into the cell by endocytosis, the vesicle is moved across the cell, and the substance is then released from the cell by exocytosis. Both endocytosis and exocytosis require energy in the form of ATP for the formation and movement of vesicles.

3.5 ORGANELLES

Learning Outcomes *After reading this section, you should be able to*

A. Describe the structure and function of the nucleus and the nucleoli.
B. Describe the structure of chromatin.
C. Compare the structure and function of rough and smooth endoplasmic reticulum.
D. Describe the roles of the Golgi apparatuses and secretory vesicles in secretion.
E. Explain the role of lysosomes and peroxisomes in digesting material taken into cells by phagocytosis.
F. Describe the structure and function of mitochondria.
G. Describe the structure and function of the cytoskeleton.
H. Describe the structure and function of centrioles.
I. Compare the structure and function of cilia, flagella, and microvilli.

Nucleus

The **nucleus** (NYU-klee-us; a little nut or the stone of a fruit) is a large organelle within the cell (see figure 3.1). All cells of the body have a nucleus at some point in their life cycle, although some cells, such as red blood cells, lose their nuclei as they mature. Other cells, such as skeletal muscle cells, contain more than one nucleus.

The contents of the nucleus is separated from the rest of the cytoplasm by a **nuclear envelope.** The nuclear envelope consists of an outer membrane and an inner membrane with a narrow space between them (figure 3.13). At many points on the surface of the nucleus, the inner and outer membranes

come together to form **nuclear pores,** passageways through which materials can move into or out of the nucleus.

Figure 3.13 APR **Nucleus**

(*a*) The nuclear envelope consists of inner and outer membranes, which become fused at the nuclear pores. The nucleolus is a condensed region of the nucleus not bounded by a membrane and consisting mostly of RNA and protein. (*b*) Transmission electron micrograph of the nucleus. (*c*) Scanning electron micrograph showing the membranes of the nuclear envelope and the nuclear pores.

(b,c) Don W. Fawcett/Science Source

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The nucleus contains most of the genetic material of the cell. This genetic material is organized into 23 pairs of **chromosomes** (KROH-moh-sohmz), which consist of DNA and proteins. During most of a cell's life, the chromosomes are loosely coiled and collectively called **chromatin** (figure 3.14; see figure 3.13*b*). When a cell prepares to divide, the chromosomes become tightly coiled and are visible when viewed with a microscope (see "Cell Cycle" later in this chapter). The genes that influence the structural and functional features of every individual are portions of DNA molecules. These

genes determine the structure of proteins and therefore direct cell structure and function.

Figure 3.14 **Structure of a Chromosome**

Chromosomes consist of DNA and proteins. When loosely coiled, chromosomes are collectively referred to as chromatin. During cell division, chromosomes become tightly coiled and visible as individual structures.

Nucleoli (noo-KLEE-oh-lie; sing. nucleolus, little nucleus) are diffuse bodies with no surrounding membrane that are found within the nucleus (see figure 3.13). There are usually one to several nucleoli within the nucleus. The subunits of ribosomes, a type of cytoplasmic organelle, are formed within a nucleolus. Figure 3.15 illustrates the production of ribosomes.

PROCESS Figure

PROCESS Figure 3.15 **Production of Ribosomes**

Ribosomal subunits are produced in the nucleus and then move into the cytoplasm, where they form ribosomes during protein synthesis.

Understand **What are the two major molecules that make up the ribosomal subunits? Recalling information from chapter 2, identify the building blocks for each of these molecule types.**

1. Proteins produced in the cytoplasm move through the nuclear pores into the nucleus and to the nucleolus.
2. These proteins are joined to **ribosomal ribonucleic** (RYE-boh-noo-KLEE-ik) **acid (rRNA),** produced within the nucleolus, to form large and small ribosomal subunits.

❸ The ribosomal subunits then move through the nuclear pores of the nuclear envelope into the cytoplasm.

❹ In the cytoplasm, one large and one small subunit join to form a ribosome during protein synthesis.

Ribosomes

Ribosomes (RYE-boh-sohmz) are the organelles where proteins are produced (see "Gene Expression" later in this chapter). Ribosomes may be attached to other organelles, such as the endoplasmic reticulum. Ribosomes that are not attached to any other organelle are called free ribosomes.

Rough and Smooth Endoplasmic Reticulum

The **endoplasmic reticulum** (EN-doh-PLAZ-mik reh-TIC-youlum; *rete,* a network) **(ER)** is a series of membranes forming sacs and tubules that extends from the outer nuclear membrane into the cytoplasm (figure 3.16). **Rough ER** is ER with attached ribosomes. A large amount of rough ER in a cell indicates that it is synthesizing large amounts of protein for export from the cell. On the other hand, ER without attached ribosomes is called **smooth ER.** Smooth ER is a site for lipid synthesis and participates in detoxification of chemicals within cells. In skeletal muscle cells, the smooth ER stores calcium ions (Ca^{2+}).

Figure 3.16 APR **Endoplasmic Reticulum**

(*a*) The endoplasmic reticulum is continuous with the nuclear envelope and can exist as either rough endoplasmic reticulum (with ribosomes) or smooth endoplasmic reticulum (without ribosomes). (*b*) Transmission electron micrograph of the rough endoplasmic reticulum.

(b) ©J. David Robertson, from Charles Flickinger, Medical Cell Biology, Philadelphia

Golgi Apparatus

The **Golgi** (GOL-jee) **apparatus,** also called the *Golgi complex*, consists of closely packed stacks of curved, membrane-bound sacs (figure 3.17). It collects, modifies, packages, and distributes proteins and lipids manufactured by the ER. For example, proteins produced at the ribosomes enter the Golgi apparatus from the ER. In some cases, the Golgi apparatus chemically modifies the proteins by attaching carbohydrate or lipid molecules to them. The proteins then are packaged into vesicles that pinch off from the margins of the Golgi apparatus. The vesicles formed at the Golgi apparatus have several destinations. For example, some, such as lysosomes, remain in the cytoplasm; some move to and are incorporated into the cell membrane; and some function as secretory vesicles (see "Secretory Vesicles"). The Golgi apparatus is present in larger numbers and is most highly developed in cells that secrete protein, such as those of the salivary glands or the pancreas.

Figure 3.17 APR **Golgi Apparatus**

(*a*) The Golgi apparatus is composed of flattened, membranous sacs and resembles a stack of dinner plates or pancakes. (*b*) Transmission electron micrograph of the Golgi apparatus.

(b) Biophoto Associates/Science Source

Secretory Vesicles

As described in "Endocytosis and Exocytosis," a vesicle is a small, membrane-bound sac that transports or stores materials within cells. Secretory vesicles pinch off from the Golgi apparatus and move to the cell membrane (figure 3.17). The membrane of a secretory vesicle then fuses with the cell membrane, and the contents of the vesicle are released to the exterior of the cell by exocytosis (see figure 3.12). In many cells, secretory vesicles accumulate in the cytoplasm and are released to the exterior when the cell receives a signal. For example, nerve cells release substances called neurotransmitters from secretory vesicles to communicate with other cells, and pancreatic cells secrete insulin in response to rising blood glucose levels.

Lysosomes and Peroxisomes

Lysosomes (LIE-soh-sohmz) are membrane-bound vesicles formed from the Golgi apparatus (figure 3.18, step 2). They contain a variety of enzymes that function as intracellular digestive systems. Figure 3.18 illustrates lysosome activity.

PROCESS Figure

PROCESS Figure 3.18 **Action of Lysosomes**

Digestive enzymes in lysosomes are used to breakdown substances.

Analyze

What is the benefit of having digestive enzymes isolated in the lysosomes as opposed to free within the cytoplasm?

1. Extracellular material is brought into the cell as a vesicle forms around the material.
2. A lysosome forms at the Golgi apparatus.
3. The lysosome moves through the cytoplasm to the vesicle and fuses with it. The enzymes in the lysosome are released into the vesicle.
4. The lysosomal enzymes mix with the material in the vesicle, and the material is broken down.

This process is seen when white blood cells phagocytize bacteria. The enzymes within lysosomes destroy the phagocytized bacteria.

Some diseases result from nonfunctional lysosomal enzymes. For example, **Pompe disease** is caused by the inability of lysosomal enzymes to break down the carbohydrate glycogen produced in certain cells. Glycogen accumulates in large amounts in the heart, liver, and skeletal muscle cells; the accumulation in heart muscle cells often leads to heart failure.

Peroxisomes (per-OK-si-sohmz) are small, membrane-bound vesicles containing enzymes that break down fatty acids, amino acids, and hydrogen peroxide (H_2O_2). Hydrogen peroxide is a by-product of fatty acid and amino acid breakdown and can be toxic to a cell. The enzymes in peroxisomes break down hydrogen peroxide to water and O_2. Cells active in detoxification, such as liver and kidney cells, have many peroxisomes.

Mitochondria

Mitochondria (my-toe-KON-dree-ah; sing. mitochondrion) are small organelles with inner and outer membranes separated by a space (figure 3.19; see figure 3.1). The outer membranes have a smooth contour, but the inner membranes have numerous folds, called **cristae** (KRIS-tee), which project into the interior of the mitochondria. The material within the inner membrane is the **mitochondrial matrix** and contains enzymes and **mitochondrial DNA (mtDNA).**

Figure 3.19 APR **Mitochondrion**
(*a*) Typical mitochondrion structure. (*b*) Transmission electron micrograph of mitochondria in longitudinal and cross sections.
(b) EM Research Services, Newcastle University

Mitochondria are the major sites of adenosine triphosphate (ATP) production within cells. Mitochondria carry out aerobic respiration (discussed in greater detail in chapter 17), a series of chemical reactions that require O_2

to break down food molecules to produce ATP. ATP is the main energy source for most chemical reactions within the cell. Cells with a large energy requirement therefore have more mitochondria than cells that require less energy. For example, cells that carry out extensive active transport, described earlier in this chapter, contain many mitochondria. Muscle cells also require large numbers of ATP for contraction. When muscles enlarge as a result of exercise, the mitochondria increase in number within the muscle cells and provide the additional ATP required for muscle contraction.

Cytoskeleton

The **cytoskeleton** (sigh-toh-SKEL-eh-ton), is the internal framework of the cell. It consists of protein structures that support the cell, hold organelles in place, and enable the cell to change shape. These protein structures are (1) microtubules, (2) microfilaments, and (3) intermediate filaments (figure 3.20).

Figure 3.20 APR **Cytoskeleton**

(*a*) Diagram of the cytoskeleton. (*b*) Scanning electron micrograph of the cytoskeleton.

(b) ©Don W. Fawcett/Science Source

Microtubules are hollow structures formed from protein subunits. The microtubules perform a variety of roles, including helping to support the

cytoplasm of cells, assisting in cell division, and forming essential components of certain organelles, such as cilia and flagella.

Microfilaments are small fibrils formed from protein subunits that structurally support the cytoplasm, determining cell shape. Some microfilaments are involved with cell movement. For example, microfilaments in muscle cells enable the cells to contract (see chapter 7).

Intermediate filaments are fibrils formed from protein subunits that are smaller in diameter than microtubules but larger in diameter than microfilaments. They provide mechanical support to the cell. A specific type of intermediate filament is **keratin,** a protein associated with skin cells (see chapter 5).

Centrioles

The **centrosome** (SEN-troh-sohm) is a specialized area of cytoplasm close to the nucleus where microtubule formation occurs. It contains two **centrioles** (SEN-tree-owlz), which are normally oriented perpendicular to each other. Each centriole is a small, cylindrical organelle composed of microtubules organized into nine triplets; each triplet consists of three parallel microtubules joined together (figure 3.21). Additional microtubules, extending from the centrosome, play an important role in cell division, as we learn later in "Mitosis."

Figure 3.21 **Centriole**

(*a*) Structure of a centriole, which is composed of nine triplets of microtubules. Each triplet contains one complete microtubule fused to two incomplete microtubules. (*b*) Transmission electron micrograph of a pair of centrioles, which are normally located together near the nucleus. One is shown in cross section and one in longitudinal section. (b) Biology Media/Science Source

Cilia, Flagella, and Microvilli

Cilia (SILL-ee-ah; sing. cilium, an eyelash) project from the surface of cells (see figure 3.1). They vary in number from none to thousands per cell and are capable of moving. Cilia are cylindrical structures that extend from the cell. Cilia are composed of microtubules, organized in a pattern similar to that of centrioles, which are enclosed by the cell membrane. Cilia are numerous on surface cells that line the respiratory tract. Their coordinated movement transports mucus, in which dust particles are embedded, upward and away from the lungs. This action helps keep the lungs clear of debris such as inhaled dust particles.

Flagella (fla-JELL-ah; sing. flagellum, a whip) have a structure similar to that of cilia but are much longer, and they usually occur only one per cell. Sperm cells each have one flagellum, which propels the sperm cell.

Microvilli (my-kroh-VIL-eye; *mikros,* small + *villus,* shaggy hair) are specialized extensions of the cell membrane that are supported by microfilaments (see figure 3.1), but they do not actively move as cilia and flagella do. Microvilli are numerous on cells that have them and they increase the surface area of those cells. They are abundant on the surface of cells that line the intestine, kidney, and other areas in which absorption is an important function.

Apply It 4

List the organelles that are plentiful in cells that (a) synthesize and secrete proteins, (b) actively transport substances into cells, and (c) ingest foreign substances by endocytosis. Explain the function of each organelle you list.

3.6 WHOLE-CELL ACTIVITY

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the process of gene expression.
B. Explain what is accomplished during mitosis.
C. Define differentiation, and explain how different cell types develop.

A cell's characteristics are ultimately determined by the types of proteins it produces. The proteins produced are in turn determined by the genetic information in the nucleus. In order to understand how a cell functions, we must consider the relationship between genes and proteins. For example, the

transport of many food molecules into the cell requires cell membrane proteins. Proteins, such as transport proteins and enzymes, are composed of specific sequences of amino acids. Information contained in DNA within the nucleus determines which types and in what sequence amino acids are combined at ribosomes to form proteins.

As you learned in the beginning of the chapter, the human body is composed of trillions of cells, with many different characteristics. Each human begins life as a single cell. Through cell division and cell differentiation, the cells that make up the human body are formed. The following sections illustrate the whole-cell activities that determine the characteristics of a functioning cell and the growth and maintenance of the human body.

Gene Expression

DNA influences the structural and functional characteristics of the entire organism because it directs protein synthesis. **Gene expression** is the process by which information stored in the genes of DNA molecules directs the manufacture of the various proteins of our cells. The proteins produced in a cell include those that serve as structural components inside the cell, proteins secreted to the outside of the cell, and enzymes that regulate chemical reactions in the cell.

A DNA molecule consists of nucleotides joined together to form two nucleotide strands (see figures 2.19 and 3.23). The two strands are connected and resemble a ladder that is twisted around its long axis. Sections of these DNA strands are called **genes,** which are sequences of nucleotides that provide a chemical set of instructions for making specific proteins. Each DNA molecule contains many different genes. You can think of a gene as the "recipe" for making a protein. How can you use this information to answer the Learn To Apply It question at the beginning of the chapter?

Gene expression involves two steps—transcription and translation, which are illustrated in figure 3.22.

PROCESS Figure

PROCESS Figure 3.22 **Overview of Gene Expression**

Gene expression involves two steps: transcription, which occurs in the nucleus, and translation, which occurs in the cytoplasm.

Analyze **In bacterial cells, translation of a mRNA can occur while it is still being transcribed from the DNA. Is this possible in our cells? Why or why not?**

❶ **Transcription** occurs in the nucleus. During this process information stored in a region of the DNA is used to produce a complementary RNA molecule, called **messenger RNA (mRNA).**

❷ The mRNA molecule moves to ribosomes in the cytoplasm where **translation** occurs. During this process, the nucleotide sequence of the molecule is used to determine the composition of a polypeptide chain, a precursor to a protein.

This process can be illustrated with an analogy. Suppose a chef wants a cake recipe that is found only in a cookbook in the library. Because the book cannot be checked out, the chef makes a copy, or transcription, of the recipe. Later in the kitchen, the information contained in the copied recipe is used to make the cake. The changing of something from one form to another (from recipe to cake) is called translation.

In terms of this analogy, DNA (the cookbook) contains many genes (recipes) for making different proteins (food items). DNA, however, is too large a molecule to pass through the nuclear pores to the ribosomes (kitchen) where the proteins are made. Just as a book stays in the library, DNA remains in the nucleus. Therefore, through transcription, the cell makes an mRNA molecule, a copy of the gene necessary to make a particular protein (figure 3.22, step 1). The mRNA then travels from the nucleus to the ribosomes in the cytoplasm, where the information in the copy is used to construct a protein by means of translation (figure 3.22, step 2). Of course, the actual ingredients are needed to turn a recipe into a cake. The ingredients necessary to synthesize a protein are amino acids. Specialized molecules, called **transfer RNAs (tRNAs),** carry the amino acids to the ribosome.

In summary, gene expression involves transcription (making a copy of a gene) and translation (converting that copied information into a protein). Next, we consider the details of transcription and translation.

Transcription

Transcription is the first step in gene expression and it takes place in the nucleus of the cell. The process of transcription is illustrated in figure 3.23.

PROCESS Figure

PROCESS Figure 3.23 APR **Formation of mRNA by Transcription of DNA**

RNA nucleotides pair with DNA nucleotides of a specific gene during transcription.

Remember **Other than the substitution of uracil for thymine in RNA, how are RNA nucleotides different from DNA nucleotides?**

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❶ DNA determines the structure of mRNA through transcription. During transcription, the double strands of a DNA segment separate.

❷ DNA nucleotides of the gene pair with RNA nucleotides that form the mRNA. Each nucleotide of DNA contains one of the following organic bases: thymine, adenine, cytosine, or guanine; each nucleotide of mRNA contains uracil, adenine, cytosine, or guanine. The number and sequence of nucleotides in the DNA serve as a template to determine the number and sequence of nucleotides in the mRNA. DNA nucleotides pair only with specific RNA nucleotides: (see figure 3.23 for specific nucleotide pairing).

❸ After the DNA nucleotides pair up with the RNA nucleotides, an enzyme catalyzes reactions that form chemical bonds between the RNA nucleotides to form a long mRNA segment. Once the mRNA segment has been transcribed, portions of the mRNA molecule may be removed.

Genetic Code

Protein synthesis relies on the cell's ability to "decode" the information stored in the nucleotide sequence of the mRNA produced during translation. The information in mRNA is carried in groups of three nucleotides called **codons,** where each codon specifies a particular amino acid. For example, the nucleotide sequence uracil, cytosine, and adenine (UCA) specifies the amino acid serine. There are 64 possible mRNA codons, but only 20 amino acids. As a result, more than 1 codon can specify the same amino acid. For example, CGA, CGG, CGU, and CGC code for the amino acid arginine. Some codons do not specify a particular amino acid but perform other functions. For example, UAA does not code for an amino acid; instead it acts as a signal to end the translation process and therefore is called a *stop* codon.

Translation

Translation is the synthesis of proteins based on the information in mRNA. Translation occurs at ribosomes (see figure 3.22, step 2). The mRNA molecules produced by transcription pass through the nuclear pores to the ribosomes. Ribosomes consist of small and large subunits, which combine with mRNA during translation. In addition to the mRNA, the process of translation requires two other types of RNA: tRNA and ribosomal RNA (rRNA). There is one type of tRNA for each mRNA codon. In each tRNA there is a three-nucleotide sequence called the **anticodon** that pairs with the codon of the mRNA. A specific amino acid is bound to another part of the tRNA. This ensures that the correct amino acid is matched with the correct codon of the mRNA. For example, the tRNA that pairs with the UUU codon of mRNA has the anticodon AAA and has the amino acid phenylalanine bound to it.

During translation, a ribosome binds to an mRNA. The ribosome aligns the mRNA with tRNA molecules so that the anticodons of tRNA can pair with the appropriate codons on the mRNA (figure 3.22, step 2). An enzyme associated with the ribosome causes the formation of a **peptide bond** between the amino acids bound to the tRNAs. The ribosome moves down the mRNA one codon at a time, releasing one of the tRNA and allowing the next tRNA to move into position. As the process continues, a **polypeptide chain** is formed. Translation ends when the ribosome reaches the stop codon on the mRNA. The polypeptide chain is released and becomes folded to form the three-dimensional structure of the protein molecule (see figure 2.19). A protein can consist of a single polypeptide chain or two or more polypeptide chains that are joined after each chain is produced on a separate ribosome.

Apply It 5

Explain how changing one nucleotide within a DNA molecule of a cell can change the structure of a protein produced by that cell.

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Cell Cycle

During growth and development, cell division allows for a dramatic increase in cell number after fertilization of an oocyte. The same process allows for the replacement and repair of damaged tissue. The cell cycle includes two major phases: a nondividing phase, called **interphase,** and cell division (figure 3.24). A cell spends most of its life cycle in interphase performing its normal functions. Interphase is divided into three phases: (1) G_1 phase, during which the cell carries out normal metabolic activity; (2) S phase, during which the DNA is replicated; and (3) G_2 phase, during which the cell prepares to divide.

Figure 3.24 APR **Cell Cycle**

The cell cycle is divided into interphase and cell division (mitosis and cytokinesis). Interphase is divided into G_1, S, and G_2 subphases. During the G_1 phase, the cell carries out routine metabolic activities. During the S phase, DNA is replicated. During the G_2 phase, the cell prepares for division. (*a*) Following mitosis, two cells are formed as the cytoplasm divides. Each new cell begins a new cell cycle. (*b*) Many cells exit the cell cycle and enter the G_0 phase, where they remain until stimulated to divide, at which point they reenter the cell cycle.

At the end of interphase, a cell has two complete sets of genetic material. The DNA is dispersed throughout the nucleus as thin threads called chromatin (figure 3.25, see also figures 3.13*b* and 3.14).

PROCESS Figure

PROCESS Figure 3.25 APR **Cell Cycle**

During interphase, DNA replication occurs, producing two copies of each chromosome. During mitosis, a cell divides, producing two new cells, each containing a complete set of chromosomes.

Ed Reschke/Photolibrary/Getty Images

A cell with the diploid number of 46 divides by mitosis. Two daughter cells are formed, one with 45 chromosomes and one with 47 chromosomes. During which phase of mitosis did the error occur that resulted in these abnormal chromosome numbers?

Cell division is the formation of daughter cells from a single parent cell. The new cells necessary for growth and tissue repair are formed through mitosis (discussed next), and the reproductive cells are formed through meiosis (discussed in chapter 19).

Each of our body cells, except for reproductive cells, contains the **diploid** (DIP-loyd) number of chromosomes, which for humans is 46. Reproductive cells have the haploid number of chromosomes, which is half the diploid number of chromosomes (see section 19.2, "Formation of Gametes"). The 46 chromosomes are organized to form 23 pairs of chromosomes. Of the 23 pairs, 1 pair is the sex chromosomes, which consist of 2 **X chromosomes** if the person is a female or an X chromosome and a **Y chromosome** if the person is a male. The remaining 22 pairs of chromosomes are called **autosomes** (AW-toh-somz) The events of each phase of mitosis are illustrated in figure 3.25.

❶ *Interphase.* During interphase, DNA exists as thin threads of chromatin. During the S phase of interphase, DNA molecules are replicated.

❷ *Prophase.* During **prophase** the chromatin condenses to form visible chromosomes each composed of the two chromatids as described above. Also during prophase, microtubules called spindle fibers extend from the centrioles. Some of these spindle fibers attach to the centromeres of each chromosome (see figures 3.1 and 3.21). The centrioles divide and migrate to each pole of the cell. In late prophase, the nucleolus and nuclear envelope disappear.

❸ *Metaphase.* In **metaphase** the chromosomes align near the center of the cell. The movement of the chromosomes is regulated by the attached spindle fibers.

❹ *Anaphase.* At the beginning of **anaphase** the chromatids separate. When this happens, each chromatid is then called a chromosome. At this point, two identical sets of 46 chromosomes are present in the cell. Each of the

two sets of 46 chromosomes is moved by the spindle fibers toward the centriole at one of the poles of the cell. At the end of anaphase, each set of chromosomes has reached an opposite pole of the cell, and the cytoplasm begins to divide.

① *Telophase.* During **telophase** (TEL-oh-fayz) the chromosomes in each of the daughter cells become organized to form two separate nuclei, one in each newly formed daughter cell. The chromosomes begin to unravel and resemble the genetic material during interphase.

② Following telophase, cytoplasm division is completed, and two separate daughter cells are produced.

Differentiation

A sperm cell and an oocyte unite to form a single cell, and a new individual begins. The single cell formed during fertilization divides by mitosis to form two cells, which divide to form four cells, and so on (see chapter 20). The trillions of cells that ultimately make up the body of an adult are derived from that single cell. Therefore, all the cells in an individual's body contain the same amount and type of DNA. But even though the genetic information contained in cells is identical, not all cells look and function alike. Bone cells, for example, do not look like or function the same as muscle cells, nerve cells, or red blood cells (figure 3.26).

Figure 3.26 **Diversity of Cell Types**
The cells of the human body show great diversity in appearance and function.

CLINICAL IMPACT

Cancer

A **tumor** (TOO-mer) is any abnormal mass of tissue that occurs within the body, usually involving cell proliferation. Tumors can be either **malignant** (mah-LIG-nant; with malice or intent to cause harm) or **benign** (bee-NINE; kind).

Benign tumors are usually less dangerous than malignant ones. They are not inclined to spread, but they may increase in size. As a benign tumor enlarges, it can compress surrounding tissues and impair their functions. In some cases (e.g., brain tumors), the results are fatal.

Malignant tumors can spread by local growth and expansion or by **metastasis** (meh-TAS-tah-sis; moving to another place), which results when tumor cells separate from the main tumor and are carried by the lymphatic system or blood vessels to a new site, where a second tumor forms.

Cancer (KAN-ser) refers to a malignant, spreading tumor and the illness that results from it. Cancers lack the normal growth control that is exhibited by most other adult tissues. Cancer results when a cell or group of cells breaks away from the normal control of growth and differentiation. This breaking loose involves the genetic machinery and can be induced by viruses, environmental toxins, and other causes. The illness associated with cancer usually occurs as the tumor invades and destroys the healthy surrounding tissues, eliminating their functions.

Promising anticancer therapies are being developed in which the cells responsible for immune responses can be stimulated to recognize tumor cells and destroy them. A major advantage in such anticancer treatments is that the cells of the immune system can specifically attack the tumor cells and not other, healthy tissues. Other therapies currently under investigation include techniques to starve a tumor to death by cutting off its blood supply. Drugs that can inhibit blood vessel development are currently in use (bevacizumab, Avastin) or under investigation (thalidomide).

Understand

Apply It 6

Cancer cells divide continuously. The normal mechanisms that regulate whether cell division occurs or ceases do not function properly in cancer cells, resulting in accelerated cell cycles. Cancer cells, such as breast cancer cells, do not look like normal, mature cells. Explain.

The process by which cells develop with specialized structures and functions is called **differentiation.** During differentiation of a cell, some portions of DNA are active, but others are inactive. The active and inactive sections of DNA differ with each cell type. For example, the portion of DNA responsible for the structure and function of a bone cell is different from that responsible for the structure and function of a muscle cell. Differentiation, then, results from the selective activation and inactivation of segments of DNA. The mechanisms that determine which portions of DNA are active in any one cell type are not fully understood, but the resulting differentiation produces the many cell types that function together to make a person. Eventually, as cells differentiate and mature, the rate at which they divide slows or even stops.

Apoptosis

Apoptosis (AP-op-TOH-sis), or *programmed cell death,* is a normal process by which cell numbers within various tissues are adjusted and controlled. In the developing fetus, apoptosis removes extra tissue, such as cells between the developing fingers and toes. In some adult tissues, apoptosis eliminates excess cells to maintain a constant number of cells within the tissue. Damaged or potentially dangerous cells, virus-infected cells, and potential cancer cells are also eliminated by apoptosis.

Apoptosis is regulated by specific genes. The proteins coded for by those genes initiate events within the cell that ultimately lead to the cell's death. As apoptosis begins, the chromatin within the nucleus condenses and fragments. This is followed by fragmentation of the nucleus and finally by death and fragmentation of the cell. Specialized cells called macrophages phagocytize the cell fragments.

EFFECTS OF A

AGING CELLS

We are all familiar with the outward signs of aging, such as wrinkled skin, gray hair, and reduced vision. A number of cellular structures or events appear to be involved in causing these effects. The major hypotheses that attempt to explain how aging occurs concentrate on molecules within the cell, such as lipids, proteins, and nucleic acids. It is estimated that at least 35% of the factors affecting aging are genetic.

One hypothesis of aging suggests the existence of a **cellular clock** that, after a certain passage of time or a certain number of cell divisions, results in the death of a given cell line.

Another hypothesis suggests that there are "death genes," which turn on late in life, or sometimes prematurely, causing cells to deteriorate and die.

Other hypotheses suggest that, through time, DNA damage, both nuclear and mitochondrial, leads to cell degeneration and death.

SUMMARY

3.1 Cell Structure

1. Cells are highly organized units containing organelles, which perform specific functions.
2. The nucleus contains genetic material, and cytoplasm is the living material between the nucleus and the cell membrane.

3.2 Functions of the Cell

1. Cells are the basic unit of life.
2. Cells protect and support the body, as well as provide for cell metabolism, communication, and inheritance.

3.3 Cell Membrane

1. The cell membrane forms the outer boundary of the cell. It determines what enters and leaves the cell.
2. The cell membrane is composed of a double layer of phospholipid molecules in which proteins float. The proteins function as membrane channels, carrier molecules, receptor molecules, enzymes, and structural components of the membrane.

3.4 Movement Through the Cell Membrane

Passive Membrane Transport

1. Diffusion is the movement of a solute from an area of higher concentration to an area of lower concentration within a solvent. At equilibrium, the distribution of molecules is uniform.
2. A concentration gradient is the concentration of a solute at one point in a solvent minus the concentration of that solute at another point in the solvent divided by the distance between the points.
3. Lipid-soluble molecules pass through the cell membrane readily by dissolving in the lipid portion of the membrane. Small molecules and ions can pass through membrane channels.
4. Osmosis is the diffusion of water across a selectively permeable membrane.
5. Osmotic pressure is the force required to prevent movement of water across a selectively permeable membrane.
6. In a hypotonic solution, cells swell (and can undergo lysis); in an isotonic solution, cells neither swell nor shrink; in a hypertonic solution, cells shrink and undergo crenation.

7. Facilitated diffusion is a mediated transport process, involving channel or carrier proteins, that moves substances from a higher to a lower concentration and does not require energy in the form of ATP.

Active Membrane Transport

1. Active transport can move substances from a lower to a higher concentration and requires ATP.
2. Secondary active transport uses the energy of one substance moving down its concentration gradient to move another substance across the cell membrane. In cotransport, both substances move in the same direction; in countertransport, they move in opposite directions.
3. Endocytosis is the movement of materials into cells by the formation of a vesicle. Receptor-mediated endocytosis involves cell receptors attaching to molecules, which are then transported into the cell. Phagocytosis is the movement of solid material into cells. Pinocytosis is similar to phagocytosis, except that the material ingested is much smaller and is in solution.
4. Exocytosis is the secretion of materials from cells by vesicle formation.

3.5 Organelles

Nucleus

1. The nuclear envelope consists of two separate membranes that form nuclear pores at many points on the surface of the nucleus.
2. DNA and associated proteins are found inside the nucleus as chromatin. DNA is the hereditary material of the cell and controls cell activities.
3. Nucleoli consist of RNA and proteins and are the sites of ribosomal subunit assembly.

Ribosomes

1. Ribosomes are the sites of protein synthesis.
2. A ribosome is composed of one large and one small subunit.

Rough and Smooth Endoplasmic Reticulum

1. Rough ER is ER with ribosomes attached. It is a major site of protein synthesis.

2. Smooth ER does not have ribosomes attached and is a major site of lipid synthesis.

Golgi Apparatus

The Golgi apparatus is a series of closely packed membrane sacs that collect, modify, package, and distribute proteins and lipids produced by the ER.

Secretory Vesicles

Secretory vesicles are membrane-bound sacs that carry substances from the Golgi apparatus to the cell membrane, where the vesicle contents are released.

Lysosomes and Peroxisomes

Lysosomes and peroxisomes are membrane-bound sacs containing enzymes. Within the cell, lysosomes break down phagocytized material. Peroxisomes break down fatty acids, amino acids, and hydrogen peroxide.

Mitochondria

Mitochondria are the major sites for the production of ATP, which cells use as an energy source. Mitochondria carry out aerobic respiration (requires O_2).

Cytoskeleton

1. The cytoskeleton supports the cytoplasm and organelles and is involved with cell movements.
2. The cytoskeleton is composed of microtubules, microfilaments, and intermediate filaments.

Centrioles

Centrioles, located in the centrosome, are made of microtubules. They facilitate chromosome movement during cell division.

Cilia, Flagella, and Microvilli

1. Cilia move substances over the surface of cells.
2. Flagella are much longer than cilia and propel sperm cells.
3. Microvilli increase the surface area of cells and thus aid in absorption.

3.6 Whole-Cell Activity

A cell's characteristics are ultimately determined by the types of proteins it produces, which are determined by the genetic information in the nucleus. Understanding how genetic information is used in the cell and distributed to daughter cells is important for understanding basic cellular activity.

Gene Expression

1. Cell activity is regulated by enzymes (proteins), and DNA controls enzyme production.
2. During transcription, the sequence of nucleotides in DNA (a gene) determines the sequence of nucleotides in mRNA; the mRNA moves through the nuclear pores to ribosomes.
3. Codons are three nucleotide sequences in mRNA that specify a particular amino acid.
4. During translation, the sequence of codons in mRNA is used at ribosomes to produce proteins. Anticodons of tRNA bind to the codons of mRNA, and the amino acids carried by tRNA are joined to form a protein.

Cell Cycle

1. The cell cycle consists of a series of events that produce new cells for growth and for tissue repair.
2. The two phases of the cell cycle are interphase and cell division.
3. DNA replicates during the S phase of interphase.
4. Cell division occurs through mitosis, which is divided into four stages:
   - Prophase—each chromosome consists of two chromatids joined at the centromere.
   - Metaphase—chromosomes align at the center of the cell.
   - Anaphase—chromatids separate at the centromere and migrate to opposite poles.
   - Telophase—the two new nuclei assume their normal structure, and cell division is completed, producing two new daughter cells.

Differentiation

Differentiation, the process by which cells develop specialized structures and functions, results from the selective activation and inactivation of DNA sections.

Apoptosis

Apoptosis is the programmed death of cells. Apoptosis regulates the number of cells within various tissues of the body.

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REMEMBERING AND UNDERSTANDING

1. Define cytoplasm and organelle.
2. List the functions of a cell.
3. Describe the structure of the cell membrane. What functions does it perform?
4. Define solution, solute, solvent, diffusion, and concentration gradient.
5. How do lipid-soluble molecules, small molecules that are not lipid-soluble, and large molecules that are not lipid-soluble cross the cell membrane?
6. Define osmosis and osmotic pressure.
7. What happens to cells that are placed in isotonic solutions? In hypertonic or hypotonic solutions? What are crenation and lysis?
8. What is carrier-mediated transport? How are facilitated diffusion and active transport similar, and how are they different?
9. How does secondary active transport work? Define cotransport and counter transport.
10. Describe receptor-mediated endocytosis, phagocytosis, pinocytosis, and exocytosis. What do they accomplish?

11. Describe the structure of the nucleus and the nuclear envelope. Name the structures in the nucleus, and give their functions.
12. Where are ribosomes assembled, and what kinds of molecules are found in them?
13. What is endoplasmic reticulum? Compare the functions of rough and smooth endoplasmic reticulum.
14. Describe the Golgi apparatus, and state its function.
15. Where are secretory vesicles produced? What are their contents, and how are they released?
16. What are the functions of lysosomes and peroxisomes?
17. Describe the structure and function of mitochondria.
18. Name the components of the cytoskeleton, and give their functions.
19. Describe the structure and function of centrioles.
20. Describe the structure and function of cilia, flagella, and microvilli.
21. Describe how proteins are synthesized and how the structure of DNA determines the structure of proteins.
22. Define autosome, sex chromosome, and diploid number.
23. How do the sex chromosomes of males and females differ?
24. Describe what happens during interphase and each stage of mitosis. What kinds of tissues undergo mitosis?
25. Define cell differentiation. In general terms, how does differentiation occur?

CRITICAL THINKING

1. The body of a man was found floating in the water of Grand Pacific Bay, which has a salt concentration slightly greater than that of body fluids. When examined

during an autopsy, the cells in his lung tissue were clearly swollen. Choose the most logical conclusion and explain your choice.

a. He probably drowned in the bay.

b. He may have been murdered elsewhere.

c. He did not drown.

2. Patients with kidney failure can be kept alive by dialysis, which removes toxic waste products from the blood. In a dialysis machine, blood flows past one side of a selectively permeable dialysis membrane, and dialysis fluid flows on the other side of the membrane. Small substances, such as ions, glucose, and urea, can pass through the dialysis membrane, but larger substances, such as proteins, cannot. If you wanted to use a dialysis machine to remove only the toxic waste product urea from blood, what could you use for the dialysis fluid? Explain your choice.

   a. a solution that is isotonic and contains only protein

   b. a solution that is isotonic and contains the same concentration of substances as blood, except for having no urea in it

   c. distilled water

   d. blood

3. Secretory vesicles fuse with the cell membrane to release their contents to the outside of the cell. In this process, the membrane of the secretory vesicle becomes part of the cell membrane. Because small pieces of membrane are continually added to the cell membrane, we would expect the cell membrane to become larger and larger as secretion continues. However, the cell membrane stays the same size. Explain how this happens.

4. Suppose that a cell has the following characteristics: many mitochondria, well-developed rough ER, well-developed Golgi apparatuses, and numerous vesicles. Predict the major function of the cell. Explain how each characteristic supports your prediction.

5. The proteins (hemoglobin) in red blood cells normally organize relative to one another, forming “stacks” of proteins that are, in part, responsible for the normal shape of red blood cells. In sickle-cell anemia, proteins inside red blood cells do not stack normally. Consequently, the red blood cells become sickle-shaped and plug up small blood vessels. Sickle-cell anemia is hereditary and results from changing one nucleotide for a different nucleotide within the gene that is responsible for producing the protein. Explain how this change results in an abnormally functioning protein.

Answers to odd-numbered critical thinking questions from this chapter appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER 4

Tissues

As we learn more about the structure of the human body, it is evident that the complexity of the body increases as we consider more structures. In this chapter we will learn how groups of cells interact to form tissues. Additionally, as illustrated in this figure, there are many subtypes of each tissue. You will also notice a pattern: form follows function. For example, in areas of the body where protection is the primary function, the tissues are dense or consist of many cell layers. On the other hand, in areas of the body where materials move across a barrier, the tissues are very thin and composed of only one cell layer.

(Pseudostratified columnar epithelium) ©Victor Eroschenko; (esophagus, medium power, adipose tissue) Alvin Telser/McGraw-Hill Education; (adipose tissue) Al Telser/McGraw-Hill Education; (human blood smear, cardiac muscle, skeletal muscle, simple squamous epithelium) ©Ed Reschke; (multipolar neuron, compact bone) ©Trent Stephens; (small intestine) Dennis Strete/McGraw-Hill

LEARN TO APPLY IT

It is Matt's birthday, but he will not be eating any cake. Matt has gluten enteropathy, also called celiac disease. Celiac disease results from an inappropriate immune response to gluten, a group of proteins found in wheat and various other grains. After eating food containing gluten, such as most breads and cereals, Matt has bouts of diarrhea because his intestinal lining is unable to properly absorb water and nutrients. The poor absorption is due to a reduced number of villi, or folds of the intestinal lining, and reduced transport capacity of the remaining cells within the villi. In chapter 3 we learned that water and nutrients enter and exit the body's cells by osmosis and other transport processes. Chapter 4 describes how tissues are specialized to allow this flow of water and nutrients.

Identify the type of tissue affected by Matt's disease and which parts of the cells in this tissue are damaged, thus reducing their ability to absorb water and nutrients. Then explain why Matt has diarrhea after eating food containing gluten.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 3 Tissues

4.1 TISSUES AND HISTOLOGY

Learning Outcomes *After reading this section, you should be able to*

A. Describe the general makeup of a tissue.

B. List the four basic tissue types.

Tissues (TISH-yous) are groups of specialized cells and the extracellular substances surrounding them. **Histology** (his-TOL-oh-jee; *histo*, tissue; *ology*, study) is the microscopic study of tissue structure. Microscopic examination of tissues can identify abnormalities, including cancer, resulting from changes in a tissue. The structure and the function of a tissue are so closely related that we can often predict the function of a tissue when given its structure, and vice versa. Knowledge of tissue structure and function is important in understanding organs, organ systems, and the complete organism. With each major tissue type, it is evident that the structure of each

tissue informs you of the function of the organ, or portion of the organ, where the tissue is found. For example, bone is our densest tissue and provides significant protection for our body. As we discuss each tissue, we will include information examining the relationship between the structure and the function of the tissue. Body tissues are classified into four types, based on the structure of the cells.

The four primary tissue types, from which all organs of the body are formed, are (1) epithelial tissue, (2) connective tissue, (3) muscle tissue, and (4) nervous tissue. Muscle and nervous tissues are more fully examined in later chapters.

4.2 EPITHELIAL TISSUE

Learning Outcomes ***After reading this section, you should be able to***

- **A.** Explain the general characteristics of epithelial tissue.
- **B.** Classify epithelial tissues based on the number of cell layers and the shape of the cells.
- **C.** Describe the various types of epithelial tissue, including their chief functions and locations.
- **D.** Relate the structural specializations of epithelial tissue with the functions they perform.
- **E.** Differentiate between exocrine and endocrine glands, and unicellular and multicellular glands.
- **F.** Categorize glands based on their structure and function.

Epithelium (ep-ih-THEE-lee-um; *epi-*, upon; *thele,* covering) is found virtually everywhere, both inside and outside the body. It is primarily a cellular tissue, meaning there is very little extracellular material between the cells. It forms the layers that cover the surfaces and line the hollow organs of our body. Epithelium is especially important in hollow organs with openings to the outside environment, because it protects against foreign materials entering the body. The characteristics common to most types of epithelial tissue are shown in figure 4.1 and listed here:

1. *Mostly composed of cells*. Epithelial tissue consists almost entirely of cells, with very little extracellular matrix between them.
2. *Covers body surfaces.* Epithelial tissue covers body surfaces and forms glands that are derived developmentally from body surfaces. The body surfaces include the exterior surface, the lining of the digestive urinary, reproductive, and respiratory tracts, the heart and blood vessels, and the linings of many body cavities.

3. *Has an exposed surface*. Because epithelial tissues form coverings and linings, one surface of their cells is in direct contact with either the outside environment or the contents of our hollow organs. For example, our skin is in contact with air in the atmosphere, and the lining of the stomach is in contact with food we eat. The surface that is exposed is called the **free surface**, or *apical* (A-pi-kal) *surface*. Epithelial cells are always oriented such that the free surface points toward the space inside a hollow organ or the external environment, even when part of a multilayered epithelial tissue. However, only the most superficial layer of cells is in contact with the environment.
4. *Attaches at the basal surface.* The surface of the cells that is anchored in place is called the **basal surface.** The basal surface is held in place through attachment to a nonliving material that is somewhat like mortar for brick. This material is called the **basement membrane** and is composed of specialized extracellular material secreted by the epithelial cells. It plays an important role in supporting and guiding cell migration during tissue repair. The basement membrane is typically porous, and regulates the movement of substances to and from the epithelial tissue above it. Epithelial cells are always oriented such that the basal surface points toward the basement membrane, even as part of a multilayered epithelial tissue. However, only the deepest layer of cells is in contact with the basement membrane. Between the epithelial cells is the **lateral surface**, where the epithelial cells are attached to each other. We will consider specialized attachments at the lateral surface later in this chapter.

5. *Has specialized cell connections and matrix attachments*. Adjacent epithelial cells are attached to each other by specialized cell connections and they are specially anchored to the extracellular matrix of the basement membrane.
6. *Is avascular.* Because of the close connections among the epithelial cells, there are no blood vessels found among the epithelial cells. In fact, the blood vessels don't penetrate the basement membrane. Instead, they lie just underneath the basement membrane, and nutrients and gases diffuse out of the blood toward the epithelial cells. In epithelial tissues with several cell layers, the outermost cells receive the nutrients and gases that have diffused through the cells in the deeper layer. Thus, the most metabolically active cells are closest to the basement membrane.
7. *Is capable of regeneration.* Epithelial tissue has the ability to replace damaged cells with new epithelial cells. Undifferentiated cells (stem cells) continuously divide and produce new cells. In some types of epithelial tissues, such as those in the skin and the digestive tract, new cells continuously replace cells that die.

Figure 4.1 **Characteristics of Epithelium**

Surface and cross-sectional views of epithelium illustrate the following characteristics: little extracellular material between cells, a free surface, and a basement membrane attaching epithelial cells to underlying tissues. The capillaries in connective tissue do not penetrate the basement membrane. Nutrients, oxygen, and waste products diffuse across the basement membrane between the capillaries and the epithelial cells.

(top) ©Victor Eroschenko; (bottom) Ed Reschke/Photolibrary/Getty Images

Functions of Epithelia

The major functions of epithelia are

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1. *Protecting underlying structures.* Examples include the outer layer of the skin and the epithelium of the oral cavity, which protect the underlying structures from abrasion.
2. *Acting as a barrier.* Epithelium prevents many substances from moving through it. For example, the epithelium of the skin acts as a barrier to water and thus reduces water loss from the body. The epithelium of the skin also prevents many toxic molecules and microorganisms from entering the body.
3. *Permitting the passage of substances.* Epithelium also allows many substances to move through it. For example, oxygen and carbon dioxide are exchanged between the air and blood by diffusion through the epithelium in the lungs.

4. *Secreting substances.* Sweat glands, mucous glands, and the enzyme-secreting portion of the pancreas are all composed of epithelial cells.
5. *Absorbing substances.* The cell membranes of certain epithelial tissues contain carrier proteins (see chapter 3) that regulate the absorption of materials. For example, the epithelial cells of the intestines absorb digested food molecules, vitamins, and ions.

Classification of Epithelia

Epithelial tissues are classified primarily according to the number of cell layers and the shape of the superficial cells. There are three major types of epithelium based on the number of cell layers in each:

1. **Simple epithelium** consists of a single layer of cells, with each cell extending from the basement membrane to the free surface.
2. **Stratified epithelium** consists of more than one layer of cells, but only the deepest layer of cells attaches to the basement membrane.
3. **Pseudostratified columnar epithelium** is a special type of simple epithelium. The prefix *pseudo-* means false, so this type of epithelium appears to be stratified but is not. It consists of one layer of cells, with all the cells attached to the basement membrane. There appear to be two or more layers of cells because some of the cells are tall and extend to the free surface, whereas others are shorter and do not extend to the free surface.

There are three types of epithelium based on idealized shapes of the epithelial cells:

1. **Squamous** (SKWAY-mus) cells are flat or scalelike.
2. **Cuboidal** (cubelike) cells are cube-shaped—about as wide as they are tall.
3. **Columnar** (tall and thin, similar to a column) cells tend to be taller than they are wide.

In most cases, an epithelium is given two names, such as simple squamous, stratified squamous, simple columnar, or pseudostratified columnar. The first name indicates the number of layers, and the second indicates the shape of the cells at the free surface (table 4.1). Table 4.2–4.3 provide an overview of the major types of epithelial tissues and their distribution.

Table 4.1 Classification of Epithelium

Number of Layers or Category	Shape of Cells

Number of Layers or Category	Shape of Cells
Simple (single layer of cells)	Squamous Cuboidal Columnar
Stratified (more than one layer of cells)	Squamous Nonkeratinized (moist) Keratinized Cuboidal (very rare) Columnar (very rare)
Pseudostratified (modification of simple epithelium)	Columnar
Transitional (modification of stratified epithelium)	Roughly cuboidal to columnar when not stretched and squamouslike when stretched

TABLE 4.2 Simple Epithelium

(a) Simple Squamous Epithelium APR

Structure:
Single layer of flat, often hexagonal cells; the nuclei appear as bumps when viewed in cross section because the cells are so flat

Function:
Diffusion, filtration, some secretion, and some protection against friction

Location:
Lining of blood vessels and the heart, lymphatic vessels, alveoli of the lungs, portions of the kidney tubules, lining of serous membranes of body cavities (pleural, pericardial, peritoneal)

(b) Simple Cuboidal Epithelium APR

Structure:

Single layer of cube-shaped cells; some cells have microvilli (kidney tubules) or cilia (terminal bronchioles of the lungs)

Function:

Secretion and absorption by cells of the kidney tubules; secretion by cells of glands and choroid plexuses; movement of particles embedded in mucus out of the terminal bronchioles by ciliated cells

Location:

Kidney tubules, glands and their ducts, choroid plexuses of the brain, lining of terminal bronchioles of the lungs, and surfaces of the ovaries

(c) Simple Columnar Epithelium APR

Structure:

Single layer of tall, narrow cells; some cells have cilia (bronchioles of lungs, auditory tubes, uterine tubes, and uterus) or microvilli (intestines)

Function:

Movement of particles out of the bronchioles of the lungs by ciliated cells; partially responsible for the movement of oocytes through the uterine tubes by ciliated cells; secretion by cells of the glands, the stomach, and the intestines; absorption by cells of the intestines

Location:

Glands and some ducts, bronchioles of lungs, auditory tubes, uterus, uterine tubes, stomach, intestines, gallbladder, bile ducts, and ventricles of the brain

(d) Pseudostratified Columnar Epithelium APR

Structure:

Single layer of cells; some cells are tall and thin and reach the free surface, and others do not; the nuclei of these cells are at different levels and appear stratified; the cells are almost always ciliated and are associated with goblet cells that secrete mucus onto the free surface

Function:

Synthesize and secrete mucus onto the free surface and move mucus (or fluid) that contains foreign particles over the surface of the free surface and from passages

Location:

Lining of nasal cavity, nasal sinuses, auditory tubes, pharynx, trachea, and bronchi of lungs

Table 4.3 Stratified Epithelium

(a) Stratified Squamous Epithelium APR

(a) Stratified Squamous Epithelium APR

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Structure:
Several layers of cells that are cuboidal in the basal layer and progressively flattened toward the surface; the epithelium can be nonkeratinized (moist) or keratinized; in nonkeratinized stratified squamous epithelium, the surface cells retain a nucleus and cytoplasm; in keratinized stratified epithelium, the cytoplasm of cells at the surface is replaced by a protein called keratin, and the cells are dead

Function:
Protects against abrasion, forms a barrier against infection, and reduces loss of water from the body

Location:
Keratinized—outer layer of the skin; nonkeratinized—mouth, throat, larynx, esophagus, anus, vagina, inferior urethra, and corneas

(b) Transitional Epithelium APR

(a) Stratified Squamous Epithelium APR

Structure: Stratified cells that appear cuboidal when the organ or tube is not stretched and squamous when the organ or tube is stretched by fluid

Function: Accommodates fluctuations in the volume of fluid in an organ or a tube; protects against the caustic effects of urine

Location: Lining of urinary bladder, ureters, and superior urethra

Simple squamous epithelium is a single layer of thin, flat cells (table 4.2*a*). Some substances easily pass through this thin layer of cells, but other substances do not.

Simple cuboidal epithelium is a single layer of cubelike cells (table 4.2*b*) that carry out active transport, facilitated diffusion, or secretion.

Simple columnar epithelium is a single layer of tall, thin cells (table 4.2*c*). The large size of these cells enables them to perform complex functions.

Pseudostratified columnar epithelium is actually a single layer of cells, but the cells appear to be layered due to the differing heights of adjacent cells and positions of their nuclei. This epithelium provides protection for the body (table 4.2*d*).

Stratified squamous epithelium forms a thick epithelium because it consists of several layers of cells (table 4.3*a*). The deepest cells are cuboidal or columnar and are capable of dividing and producing new cells. As these newly formed cells are pushed to the surface, they become flat and thin.

Transitional epithelium is a special type of stratified epithelium that can stretch (table 4.3*b*). In the unstretched state, transitional epithelium consists of five or more layers of cuboidal or columnar cells. As transitional

epithelium is stretched, the cells flatten, and the number of cell layers decreases. Transitional epithelium lines cavities that expand, such as the urinary bladder.

The Relationship Between Structure and Function of Epithelial Tissues

Number of Cell Layers and Cell Shapes

As the number of cell layers increases and the shape of the cells becomes more robust, we see a proportional increase in the degree of protection an epithelial tissue provides and increased complexity of the function it performs.

1. *One layer of flat cells*. Simple squamous epithelium is best adapted for areas of the body where filtration and diffusion are common. For example, simple squamous epithelium in the air sacs in the lungs allows diffusion of gases between the air and blood. In the kidneys, simple squamous epithelium in special structures allows wastes, but not blood cells, to be filtered from the blood. In addition, simple squamous epithelium protects organs in the pericardial, pleural, and peritoneal cavities (see chapter 1) by covering them with a thin, lubricated layer of tissue to allow the organs to easily slide past each other without friction-induced damage occurring.
2. *One layer of cubelike cells.* Simple cuboidal epithelium, due to the larger volume of these cells, has a greater secretory capacity than simple squamous epithelium. In fact, most glands in the body and other secretory structures are frequently composed of simple cuboidal epithelium. Additionally, the larger size of cuboidal cells can create tubes that are sturdy and provide more protection than tubes composed of simple squamous epithelium.
3. *One layer of tall, rectangular cells.* Simple columnar epithelial cells are much taller than those of cuboidal epithelium. Draw a sketch of squamous, cuboidal, and columnar epithelial cells side-by-side. Which cell type provides the thickest barrier? Simple columnar epithelium of the small intestine produces digestive enzymes, absorbs nutrients, and secretes mucus, which protects the lining of the intestine. Also, because these cells are tall, bacteria cannot easily penetrate the lining of the intestine. Pseudostratified columnar epithelium, like simple columnar, is composed of tall cells and secretes mucus, which provides protection such as trapping inhaled debris in the trachea.
4. *Multiple layers of flat cells.* Stratified squamous epithelium forms a thick barrier, which can be as many as 30–40 cells thick. One type of stratified squamous epithelium forms the outer layer of the skin, contains the protein

keratin, and is called keratinized stratified squamous epithelium (see chapter 5). The thick layer of cells provides protection against abrasion, and forms a barrier that protects against water loss and prevents microorganisms and toxic chemicals from entering the body. In contrast, nonkeratinized stratified squamous epithelium, such as is found in the mouth and throat, has a moist surface, but also provides protection against abrasion by acting as a mechanical barrier. However, water can move across this epithelium more readily than across the skin.

CLINICAL IMPACT

Effect of Smoking on Air Passageway Epithelium

The shape and number of layers of epithelial cells can change if they are subjected to long-term irritation or other abnormal conditions. People who smoke cigarettes eventually experience changes in the epithelium of the larger airways. The delicate pseudostratified columnar epithelium, which performs a cleaning function by moving mucus and debris from the passageways, is replaced by stratified squamous epithelium, which is more resistant to irritation but does not perform a cleaning function. Also, lung cancer most often results from changes in epithelial cells in the lung passageways of smokers. The cancer is identified by the changes in cell structure.

There are types of epithelial tissues that consist of multiple layers of cuboidal and columnar cells. These are more rare but generally provide a greater level of protection and strength to structures in which they are found.

Apply It 1

Explain the consequences of having (a) nonkeratinized stratified epithelium rather than simple columnar epithelium lining the digestive tract and (b) nonkeratinized stratified squamous epithelium rather than keratinized stratified squamous epithelium at the surface of the skin.

Free Surface Modifications

The free surfaces of epithelial tissues are not in contact with other cells and can be smooth or folded. They may also have microvilli or cilia (see chapter 3). Smooth free surfaces reduce friction; an example of such a surface is the tissue lining blood vessels. This kind of tissue is a specialized type of simple squamous epithelium called **endothelium** (see chapter 13).

Folded free surfaces have increased surface area. Microvilli are stationary and are found in cells that absorb or secrete, such as the lining of the small intestine (see chapter 16). This information may be helpful to you in answering the Learn to Apply It question at the beginning of this chapter. In contrast, cilia are not stationary—instead they can move, which allows them to remove from the respiratory airways mucus that contains foreign particles. The mucus is moved toward the throat, where it is swallowed, and the foreign particles are degraded by acid in the stomach (see chapter 15). Cilia are also found on the free surfaces of the simple columnar epithelial cells of the uterus and uterine tubes, where the cilia help move mucus and oocytes (eggs).

Cell Connections

Cells have structures that hold them to each other or to the basement membrane. These structures do three things: (1) mechanically bind the cells together, (2) help form a barrier to the movement of molecules or ions, and (3) provide a mechanism for intercellular communication (figure 4.3).

Nonkeratinized stratified squamous epithelial cell
Free surface
Nuclei
Basement membrane
LM 72x
Stratified squamous epithelium
Basement membrane
Transitional epithelial cell
Nucleus
Free surface
LM 413x
Transitional epithelium

Free surface
Tight junction
Adhesion belt
Actin filaments
Desmosome
Channel

Figure 4.3 **Cell Connections**

This figure depicts the cell connections discussed in this chapter. There are not many cells in the body that would possess all of these types of connections. Cells can be anchored to each other by desmosomes, adhesion belts, or tight junctions, whereas hemidesmosomes anchor cells to the basement membrane. Gap junctions allow adjacent cells to communicate with each other.

Cell connection structures that mechanically bind epithelial cells together are called **desmosomes** (DEZ-mo-somes); *desmos,* a band; *soma,* body), while those that bind cells to the basement membrane are called **hemidesmosomes** (HEM-ee-dez-moh-sohms; *hemi,* half). Both types of mechanical linkages consist of adhesive material between the cells and intermediate filaments that extend into the cytoplasm of adjacent cells. Many desmosomes are found in epithelial tissues subjected to mechanical stress, such as the stratified squamous epithelium of the skin. Hemidesmosomes are the anchors of epithelial tissues to the underlying basement membrane, preventing the movement of the tissue.

Tight junctions are cell connection structures that (1) form barriers and (2) anchor cells to each other. Tight junctions form a barrier to movement of molecules or ions between epithelial cells. In addition, tight junctions anchor cells together. Structures called **adhesion belts** are found just below the tight junctions, and help the tight junctions anchor the epithelial cells to each other. Tight junctions are located near the free surface of the epithelial cells and form rings that completely surround each cell. These arrangements bind adjacent cells together to prevent passage of materials between cells. Thus the name *tight* junctions. For example, in the stomach and urinary bladder, chemicals cannot pass between cells—water and other substances must pass through the epithelial cell membranes. This allows tight regulation of what is absorbed or secreted. The adhesion belt provides additional strength for the binding of cells together at locations of tight junctions.

Cell connection structures that allow for intercellular communication include **gap junctions.** Gap junctions consist of groups of channels that

allow small molecules and ions to pass from one epithelial cell to an adjacent one. Although most epithelial cells are connected to each other by gap junctions, the function of gap junctions in epithelial tissue is not entirely clear; gap junctions between cells of ciliated epithelial tissue may coordinate movement of the cilia. However, gap junctions between cells of other tissues have well-known functions. In cardiac and smooth muscle, electrical signals are passed from cell to cell through gap junctions, which allows for coordinated contraction (see chapter 7).

Glands

Now that you've learned that many epithelial tissues are capable of secretion, let's examine specialized secretory organs, called glands. **Glands** are composed of epithelium supported by a network of connective tissue. There are two major types of glands in the body: (1) endocrine glands, and (2) exocrine glands.

Endocrine glands produce chemicals called **hormones** and are often termed ductless glands based on their structure and mode of secretion. These glands are associated with an extensive network of blood vessels, and their hormones are transported throughout the body by way of the blood. Hormones are discussed in more detail in chapter 10.

Figure 4.2 **Epithelial Tissue**

The two main types of epithelial tissues are simple and stratified. Within these two categories, cell shape determines the specific epithelial tissue and influences the function.

(Pseudostratified, simple columnar, simple columnar, simple cuboidal, Stratified squamous, Transitional epithelium) ©Victor Eroschenko; (Simple squamous) Alvin Telser/McGraw-Hill Education

Exocrine glands produce a wide variety of products, such as saliva, sweat, and digestive tract secretions. These secretions enter ducts, which are continuous with the epithelial tissue surface. At the appropriate location, the secretions exit onto the free surface of the target organ's tissue. Exocrine

glands are primarily categorized on the basis of their structure, but they are also separated on the basis of their mode of secretion. For example, there are exocrine glands that have the same structure but utilize different modes of secretion. By the same token, there are glands that utilize the same mode of secretion but have very different structures.

The three specific distinctions we use in this textbook are (1) structure of the duct, (2) structure of the secretory portion of the gland, and (3) mode of secretion within the secretory portion (figure 4.4).

Figure 4.4 **Structure of Exocrine Glands**

(*a*) Unicellular glands. Exocrine glands can be unicellular, but are most often multicellular. (*b*) Simple glands. These have single, nonbranched ducts. (*c*) Compound glands. These have multiple, branched ducts. (*d*) Modes of secretion: merocrine glands, apocrine glands, and holocrine glands.

Structure of Exocrine Glands

First, it's important to distinguish between the duct and the secretory portion of the gland. The duct refers to the tube in contact with the epithelial tissue

free surface, which transports the secreted material. Second, the secretory portion of the gland is found deeper in the epithelium and is composed of the cells responsible for producing the secreted material. The three major categories of exocrine glands are (1) unicellular, (2) simple, and (3) compound.

Unicellular

Some exocrine glands are composed of only a single cell, such as **goblet cells** that secrete mucus (figure 4.4*a*, table 4.4).

Table 4.4 Representative Exocrine Glands

Structure	Structural Subtype	Example	Mode of Secretion
Unicellular	----	Goblet Cell	Merocrine
Multicellular Simple	Simple tubular	Glands in stomach	Merocrine
	Simple branched tubular	Gastric glands in stomach	Merocrine
	Simple acinar	Sebaceous glands	Holocrine
	Simple branched acinar	Thyroid gland	Merocrine
Compound	Compound tubular	Mucous glands of duodenum	Merocrine
	Compound acinar	Mammary glands	Apocrine for fatty portion
	Compound tubuloacinar	Pancreas	Merocrine for protein-rich portion
			Merocrine

Simple

Simple glands are multicellular glands that have a single, nonbranched duct (figure 4.4*b*, see table 4.4). The secretory portions of the gland can be shaped in one of two ways: (1) **tubular,** which is a straight, narrow tube the same width as the duct, or (2) **acinar,** a saclike structure whose width is greater than the width of the duct. We see several different types of simple glands.

- *Simple tubular*—glands forming a straight tube with no branching of the secretory portion
- *Simple branched tubular*—gland with several tubular secretory portions branching from the single duct
- *Simple acinar*—glands with a single saclike secretory portion
- *Simple branched acinar*—glands with several acinar secretory portions branching from the single duct

Compound

Compound glands are multicellular glands that have several branched ducts (figure 4.4*c*; see table 4.4). Again, the secretory portions can be either tubular or acinar, or a mixture of both.

- *Compound tubular*—glands with multiple ducts, each with a narrow tubular secretory portion
- *Compound acinar*—glands with multiple ducts, each with several saclike secretory portions
- *Compound tubuloacinar*—glands with multiple ducts, each with several tubular and acinar secretory portions

Modes of Secretion by Exocrine Glands

Within each of the structural categories, the cells of the secretory portion may use one of three modes of secretion or even a combination of secretion modes (figure 4.4*d*). The three modes are (1) merocrine, (2) apocrine, and (3) holocrine.

Merocrine (MARE-oh-krin; *mero,* partial; *crine,* to separate) **secretion** is the release of secretory products through exocytosis and is the most common. For example, merocrine secretion is used by goblet cells, temperature-sensitive sweat glands, and the exocrine portion of the pancreas.

Apocrine (AP-oh-krin; *apo,* away from) **secretion** is the release of secretory products when a portion of the free surface of the epithelial cell pinches off, releasing cytoplasmic contents. The remainder of the cell is repaired. Release of the fatty portion of milk by mammary glands occurs through apocrine secretion, as does secretion of earwax.

Holocrine (HOL-oh-kryn; *holos*, whole) **secretion** is the release of secretory products through shedding of entire cells. Once the secretory products have accumulated in the epithelial cell, the cell disintegrates and becomes part of the secretion. Deeper cells in the gland replace lost cells. Sebaceous (oil) glands in the skin release sebum (oil) through holocrine secretion, which can help explain the appearance of blackheads. The dark-colored material of a blackhead is sometimes mistaken for dirt, but it is actually melanin from the disintegrated cell. Changes in hormones are the principal causes of blackhead formation, not necessarily the frequency with which a person washes their face.

4.3 CONNECTIVE TISSUE

Learning Outcomes *After reading this section, you should be able to*

A. Describe the classification of connective tissue.
B. Give examples of each major type.

Connective tissue is a diverse primary tissue type that makes up part of every organ in the body. Connective tissue differs from the other three tissue types in that it consists of cells separated from each other by abundant extracellular matrix. Connective tissue is diverse in both structure and function.

Functions of Connective Tissue

Connective tissue performs the following major functions:

1. *Enclosing and separating other tissues.* Sheets of connective tissue form capsules around organs, such as the liver and the kidneys. Connective tissue also forms layers that separate tissues and organs. For example, connective tissues separate muscles, arteries, veins, and nerves from one another.
2. *Connecting tissues to one another.* Tendons are strong cables, or bands, of connective tissue that attach muscles to bone, and ligaments are connective tissue bands that hold bones together.
3. *Supporting and moving parts of the body.* Bones of the skeletal system provide rigid support for the body, and semirigid cartilage supports structures, such as the nose, the ears, and the surfaces of joints. Joints between bones allow one part of the body to move relative to other parts.
4. *Storing compounds.* Adipose tissue (fat) stores high-energy molecules, and bones store minerals, such as calcium and phosphate.
5. *Cushioning and insulating.* Adipose tissue cushions and protects the tissues it surrounds and provides an insulating layer beneath the skin that helps conserve heat.
6. *Transporting.* Blood transports gases, nutrients, enzymes, hormones, and cells of the immune system throughout the body.
7. *Protecting.* Cells of the immune system and blood provide protection against toxins and tissue injury, as well as against microorganisms. Bones protect underlying structures from injury.

Cells of Connective Tissue

The specialized cells of the various connective tissues produce the extracellular matrix. The name of the cell identifies the cell functions by

means of one of the following suffixes: *-blast, -cyte, or -clast*. **Blasts** create the matrix, **cytes** maintain it, and **clasts** break it down for remodeling. For bone, **osteoblasts** (*osteo-*, bone) form it, **osteocytes** maintain it, and **osteoclasts** break it down (see chapter 6). For fibrous connective tissue, **fibroblasts** form it, and **fibrocytes** maintain it. For cartilage, **chondroblasts** form it (*chondro-,* cartilage), and **chondrocytes** maintain it.

Also found in connective tissue are cells associated with the immune system. **Macrophages** (MAK-roh-fay-jes; *makros,* large + *phago,* to eat) are large white blood cells that are capable of moving about and ingesting foreign substances, including microorganisms in the connective tissue. **Mast cells** are nonmotile cells that release chemicals, such as histamine, that promote inflammation.

Extracellular Matrix

The extracellular matrix of connective tissue has three major components: (1) protein fibers, (2) ground substance, and (3) fluid. Ground substance consists of nonfibrous protein and other molecules. The structure of the matrix is responsible for the functional characteristics of connective tissues—for example, they enable bones and cartilage to bear weight, tendons and ligaments to withstand tension, and the skin's dermis to withstand punctures, abrasions, and other abuse.

Protein Fibers of the Matrix

Three types of protein fibers—(1) collagen, (2) reticular, and (3) elastic—help form most connective tissues. **Collagen** (KOL-ah-jen; glue-producing) **fibers,** which resemble microscopic ropes, are very flexible but resist stretching. **Reticular** (reh-TIK-you-lar) **fibers** are very fine, short collagen fibers that branch to form a supporting network. **Elastic fibers** have the ability to return to their original shape after being stretched or compressed, giving tissue an elastic quality. This tissue stretches like a rubber band in response to force and recoils when relaxed.

Ground Substance of the Matrix

The **ground substance** consists of nonfibrous molecules. It is the "shapeless" background against which the collagen fibers are seen through the microscope. **Proteoglycans** (PROH-tee-oh-GLYE-kans; *proteo,* protein + *glycan,* polysaccharide) are large molecules that consist of a protein core attached to many long polysaccharides. The amount of fluid in the matrix is

correlated with the type and quantity of ground substance molecules. For example, proteoglycans trap large quantities of water between the polysaccharides, which allows them to return to their original shape when compressed or deformed.

Classification of Connective Tissue

Connective tissue types blend into one another, and the transition points cannot be identified precisely. As a result, connective tissue is somewhat arbitrarily classified by the type and proportions of cells and extracellular matrix.

The two main types of connective tissue are embryonic and adult connective tissue. By eight weeks of development, most of the embryonic connective tissue has become specialized to form the types of connective tissue seen in adults.

Table 4.5 presents the classification of adult connective tissue used in this text. Adult connective tissue consists of three types: (1) connective tissue proper (loose and dense), (2) supporting connective tissue (cartilage and bone), and (3) fluid connective tissue (blood).

Table 4.5 Classification of Connective Tissues
Connective tissue proper Loose (fewer fibers, more ground substance) Areolar Adipose Reticular Dense (more fibers, less ground substance) Dense, regular collagenous Dense, regular elastic Dense, irregular collagenous (not shown) Dense, irregular elastic (not shown)
Supporting connective tissue Cartilage (semisolid matrix) Hyaline Fibrocartilage Elastic Bone (solid matrix) Spongy Compact
Fluid connective tissue Blood

Connective Tissue Proper

Loose Connective Tissue

Loose connective tissue (table 4.6) consists of relatively few protein fibers that form a lacy network, with numerous spaces filled with ground substance and fluid. Three subdivisions of loose connective tissue are (1) areolar, (2) adipose, and (3) reticular. The extracellular matrix of **areolar** (ah-REE-oh-lar) connective tissue primarily consists of collagen fibers and a few elastic fibers. The most common cells in loose connective tissue are the fibroblasts. Fibroblasts are responsible for producing the matrix. Loose connective tissue is widely distributed throughout the body. It cushions most organs and other tissues; it attaches the skin to underlying tissues and provides nourishment for the structures with which it is associated (table 4.6*a*). The basement membranes of epithelia often rest on loose connective tissue.

Table 4.6	Connective Tissue Proper: Loose Connective Tissue
(a) Areolar Connective Tissue APR	

(a) Areolar Connective Tissue APR

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Structure:

A fine network of fibers (mostly collagen fibers with a few elastic fibers) with spaces between the fibers; fibroblasts, macrophages, and lymphocytes are located in the spaces

Function:

Loose packing, support, and nourishment for the structures with which it is associated

Location:

Widely distributed throughout the body; substance on which epithelial basement membranes rest; packing between glands, muscles, and nerves; attaches the skin to underlying tissues

(b) Adipose Tissue APR

(a) Areolar Connective Tissue APR

©Ed Reschke

Structure:
Little extracellular matrix surrounding cells; the adipocytes, or fat cells, are so full of lipid that the cytoplasm is pushed to the periphery of the cell

Function:
Packing material, thermal insulator, energy storage, and protection of organs against injury from being bumped or jarred

Location:
Predominantly in subcutaneous areas, mesenteries, renal pelves, around kidneys, attached to the surface of the colon, mammary glands, and in loose connective tissue that penetrates into spaces and crevices

(c) Reticular Tissue APR

(a) Areolar Connective Tissue APR

Al Telser/McGraw-Hill Education

Structure:
Fine network of reticular fibers irregularly arranged

Function:
Provides a superstructure for lymphatic and hemopoietic tissues

Location:
Within the lymph nodes, spleen, bone marrow

Adipose (ADD-i-pose; fat) tissue consists of adipocytes, or fat cells, which contain large amounts of lipids for energy storage. Unlike other connective tissue types, adipose tissue is composed of large cells and a small amount of extracellular matrix, which consists of loosely arranged collagen and reticular fibers with some scattered elastic fibers. The individual cells are large and closely packed together (table 4.6*b*). Adipose tissue also pads and protects parts of the body and acts as a thermal insulator.

Reticular tissue forms the framework of lymphatic tissue, such as in the spleen and lymph nodes, as well as in bone marrow and the liver (table 4.6*c*).

Dense Connective Tissue

Dense connective tissue has a relatively large number of protein fibers that form thick bundles and fill nearly all of the extracellular space. These protein fibers are produced by fibroblasts. There are two major subcategories of dense connective tissue: (1) collagenous and (2) elastic.

Dense collagenous connective tissue has an extracellular matrix consisting mostly of collagen fibers (table 4.7*a*). Structures made up of dense collagenous connective tissue include tendons, which attach muscle to bone; many ligaments, which attach bones to other bones; and much of the dermis, which is the connective tissue of the skin. Dense collagenous connective tissue also forms many capsules that surround organs, such as the liver and kidneys. In tendons and ligaments, the collagen fibers are oriented in the same direction, and so the tissue is called **dense regular,** but in the dermis and in organ capsules, the fibers are oriented in many different directions, and so the tissue is called **dense irregular.**

Apply It 2

In tendons, collagen fibers are oriented parallel to the length of the tendon. In the skin, collagen fibers are oriented in many directions. What are the functional advantages of the fiber arrangements in tendons and in the skin?

Dense elastic connective tissue has abundant elastic fibers among its collagen fibers. The elastic fibers allow the tissue to stretch and recoil. Examples include the dense elastic connective tissue in the vocal cords (table 4.7*b*), in elastic ligaments, and in the walls of large arteries. The elastic fibers are oriented in the same direction in elastic ligaments and in the vocal cords (dense regular tissue), but they are oriented in many different directions in the walls of arteries (dense irregular tissue; not pictured). A genetic condition called Marfan syndrome results from, in part, the inability to properly maintain and form elastic fibers. Because elastic fibers are found in connective tissue throughout the body, multiple body systems are affected. However, the major cause of death from Marfan syndrome is weakening and rupture of the aorta wall.

Table 4.7	Connective Tissue Proper: Dense Connective Tissue
(a) Dense Regular Collagenous Connective Tissue APR	

(a) Dense Regular Collagenous Connective Tissue APR

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Structure:
Matrix composed of collagen fibers running in somewhat the same direction in tendons and ligaments; collagen fibers run in several directions in the dermis of the skin and in organ capsules

Function:
Withstand great pulling forces exerted in the direction of fiber orientation due to great tensile strength and stretch resistance

Location:
Tendons (attach muscle to bone) and ligaments (attach bones to each other); also found in the dermis of the skin, organ capsules, and the outer layer of many blood vessels

(b) Dense Regular Elastic Connective Tissue APR

(a) Dense Regular Collagenous Connective Tissue APR

Structure: Matrix composed of collagen fibers and elastin fibers running in somewhat the same direction in elastic ligaments; elastic fibers run in connective tissue of blood vessel walls

Function: Capable of stretching and recoiling like a rubber band with strength in the direction of fiber orientation

Location: Elastic ligaments between the vertebrae and along the dorsal aspect of the neck (nucha) and in the vocal cords; also found in elastic connective tissue of blood vessel walls

Apply It 3

Scars consist of dense connective tissue made of collagen fibers. Vitamin C is required for collagen synthesis. Predict the effect of scurvy, a nutritional disease caused by vitamin C deficiency, on wound healing.

Supporting Connective Tissue

Cartilage

Cartilage (KAR-tih-lij) is composed of **chondrocytes** (KON-droh-sites), or cartilage cells, located in spaces called **lacunae** (la-KOO-nee; small spaces) within an extensive matrix (table 4.8). Collagen in the matrix gives cartilage flexibility and strength. Cartilage is resilient because proteoglycans in the matrix trap water. This makes cartilage relatively rigid but still able to spring back after being compressed. Cartilage provides support, while allowing flexibility. However, because blood vessels do not penetrate the interior of cartilage structures, cartilage heals slowly after an injury. Cells and nutrients necessary for tissue repair do not reach the damaged area.

Table 4.8	Supporting Connective Tissue: Cartilage
(a) Hyaline Cartilage APR	

(a) Hyaline Cartilage APR

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Structure:
Collagen fibers are small and evenly dispersed in the matrix, making the matrix appear transparent; the chondrocytes are found in spaces, or lacunae, within the firm but flexible matrix

Function:
Allows growth of long bones; provides rigidity with some flexibility in the trachea, bronchi, ribs, and nose; forms strong, smooth, yet somewhat flexible articulating surfaces; forms the embryonic skeleton

Location:
Growing long bones, cartilage rings of the respiratory system, costal cartilage of ribs, nasal cartilages, articulating surface of bones, and the embryonic skeleton

(b) Fibrocartilage APR

(a) Hyaline Cartilage APR

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Structure:
Collagen fibers similar to those in hyaline cartilage; the fibers are more numerous than in other cartilages and are arranged in thick bundles

Function:
Somewhat flexible and capable of withstanding considerable pressure; connects structures subjected to great pressure

Location:
Intervertebral disks, pubic symphysis, and articular disks (e.g., knees and temporomandibular [jaw] joints)

(c) Elastic Cartilage APR

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Structure:
Similar to hyaline cartilage, but matrix also contains elastic fibers

Function:
Provides rigidity with even more flexibility than hyaline cartilage because elastic fibers return to their original shape after being stretched

Location:
External ears, epiglottis, and auditory tubes

There are three types of cartilage:

1. **Hyaline** (HIGH-ah-lin; clear or glassy) **cartilage** (see table 4.8*a*) is the most abundant type of cartilage and has many functions. It covers the ends of bones where they come together to form joints. In joints, hyaline cartilage forms smooth, resilient surfaces that can withstand repeated compression. Hyaline cartilage also forms the cartilage rings of the respiratory tract, the nasal cartilages, and the costal cartilages, which attach the ribs to the sternum (breastbone).
2. **Fibrocartilage** (table 4.8*b*) has more collagen than does hyaline cartilage, and bundles of collagen fibers can be seen in the matrix. Fibrocartilage can withstand both compression and pulling or tearing forces. Fibrocartilage is found in the disks between the vertebrae (bones of the back) and in some joints, such as the knee and temporomandibular (jaw) joints.
3. **Elastic cartilage** (table 4.8*c*) contains elastic fibers in addition to collagen and proteoglycans. The elastic fibers appear as coiled fibers among bundles of collagen fibers. Elastic cartilage is able to recoil to its original shape when bent. The external ear, epiglottis, and auditory tube contain elastic cartilage.

Bone

Bone is a hard connective tissue that consists of living cells and a mineralized matrix (table 4.9; see chapter 6). Osteocytes (*osteo,* bone), or bone cells, are located within lacunae. The strength and rigidity of the mineralized matrix enables bones to support and protect other tissues and organs. Two types of bone tissue exist:

Table 4.9 Supporting Connective Tissue: Bone

Structure: Hard, bony matrix predominates; many osteocytes (not seen in this bone preparation) are located within lacunae; the matrix is organized into layers called lamellae

Function: Provides great strength and

	support and protects internal organs, such as the brain; bone also provides attachment sites for muscles and ligaments; the joints of bones allow movements **Location:** All bones of the body

1. **Spongy bone** has spaces between **trabeculae** (trah-BEK-you-lee), or plates, of bone and therefore resembles a sponge (table 4.9).
2. **Compact bone** is more solid, with almost no space between many thin layers of mineralized matrix (table 4.9).

Fluid Connective Tissue

Blood

Blood is unique because the matrix is liquid, enabling blood cells and platelets, collectively called **formed elements,** to move through blood vessels (table 4.10). Some formed elements even leave the blood and migrate into other tissues. The liquid matrix enables blood to flow rapidly through the body, carrying nutrients, O_2, waste products, and other materials. Blood is discussed more fully in chapter 11.

Table 4.10 Fluid Connective Tissue: Blood

Structure:
Formed elements and a fluid matrix

Function:
Transports oxygen, carbon dioxide, hormones, nutrients, waste products, and other substances;

	protects the body from infections and is involved in temperature regulation **Location:** Within the blood vessels; white blood cells frequently leave the blood vessels and enter the extracellular spaces

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4.4 MUSCLE TISSUE

Learning Outcomes ***After reading this section, you should be able to***

A. Discuss the three types of muscle tissue.
B. Describe the general structure, location in the body, and function of each muscle type.

The main function of **muscle tissue** is to contract, or shorten, making movement possible. Muscle contraction results from contractile proteins located within the muscle cells, called **muscle fibers** (see chapter 7).

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Connective Tissue Proper
Loose Connective Tissue
Nucleus
Elastic fiber
Collagen fiber
LM 400x
Areolar connective tissue (under skin)
Nucleus
Fat cells
LM 100x
Adipose (around muscle)
Leukocytes
Reticular fibers
LM 280x
Reticular tissue (bone marrow)
Dense Connective Tissue
Nucleus of fibroblast
Collagen fibers
LM 1000x
Dense regular connective tissue (tendon)
Elastic fibers
Nucleus of fibroblast
LM 200x
Dense regular elastic connective tissue (wall of aorta)
Fluid Connective Tissue
Platelets
Red blood cells
White blood cells
LM 400x
Blood

Figure 4.5 **Connective Tissue**

The three main types of connective tissues are connective tissue proper, supporting connective tissue, and fluid connective tissue. Within these three categories, cell type and extracellular matrix composition determine the specific connective tissue and influence the function.

(Areolar) ©Ed Reschke; (Adipose) ©Ed Reschke; (Reticular) Al Telser/McGraw-Hill Education; (Collagenous) Ed Reschke/Stone/Getty Images; (Elastic) ©Victor Eroschenko; (Fluid connective) Ed Reschke/Getty Images; (Elastic, hypaline, fibrocartilage) Victor P. Eroschenko; (Supporting tissue) ©Trent Stephens

The three types of muscle tissue are (1) skeletal, (2) cardiac, and (3) smooth. **Skeletal muscle** is what we normally think of as "muscle" (table 4.11*a*). It is the meat of animals and constitutes about 40% of a person's body weight. As the name implies, skeletal muscle attaches to the skeleton and enables the body to move. Skeletal muscle is described as voluntary (under conscious control) because a person can purposefully cause skeletal muscle contraction to achieve specific body movements. However, the nervous system can cause skeletal muscles to contract without conscious involvement, as occurs during reflex movements and the maintenance of muscle tone. Skeletal muscle cells tend to be long and cylindrical, with several nuclei per cell. Some skeletal muscle cells extend the length of an entire muscle. Skeletal muscle cells are **striated** (STRI-ate-ed), or banded, because of the arrangement of contractile proteins within the cells.

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Table 4.11 Muscle Tissue

(a) Skeletal Muscle APR

Structure: Skeletal muscle cells or fibers appear striated (banded); cells are large, long, and cylindrical, with many nuclei

Function: Movement of the body; under voluntary control

Location: Attached to bone or other connective tissue

(b) Cardiac Muscle APR

(a) Skeletal Muscle APR

Structure:
Cardiac muscle cells are cylindrical and striated and have a single nucleus; they are branched and connected to one another by intercalated disks, which contain gap junctions

Function:
Pumps the blood; under involuntary (unconscious) control

Location:
In the heart

(c) Smooth Muscle APR

(a) Skeletal Muscle APR

Structure: Smooth muscle cells are tapered at each end, are not striated, and have a single nucleus

Function: Regulates the size of organs, forces fluid through tubes, controls the amount of light entering the eye, and produces "goose bumps" in the skin; under involuntary (unconscious) control

Location: In hollow organs, such as the stomach and intestine; skin and eyes

Apply It 4

Given that skeletal muscle fibers are responsible for doing the work of contracting to regulate movement, which organelle do you think is found in particularly high numbers in these cells?

Cardiac muscle is the muscle of the heart; it is responsible for pumping blood (table 4.11*b*). Cardiac muscle is under involuntary (unconscious) control, although a person can learn to influence the heart rate by using techniques such as meditation and biofeedback. Cardiac muscle cells are cylindrical but much shorter than skeletal muscle cells and are striated, with one nucleus per cell. They are often branched and connected to one another by **intercalated** (in-TER-kah-lay-ted) **disks.** The intercalated disks, which

contain specialized gap junctions, are important in coordinating the contractions of the cardiac muscle cells (see chapter 12).

Smooth muscle forms the walls of hollow organs (except the heart); it is also found in the skin and the eyes (table 4.11c). Smooth muscle is responsible for a number of functions, such as moving food through the digestive tract and emptying the urinary bladder. Like cardiac muscle, smooth muscle is controlled involuntarily. Smooth muscle cells are tapered at each end, have a single nucleus, and are not striated.

Apply It 5

Make a table that summarizes the characteristics of the three major muscle types. The muscle types should form a column at the left side of the table, and the characteristics of muscle should form a row at the top of the table.

4.5 NERVOUS TISSUE

Learning Outcomes *After reading this section, you should be able to*

A. Describe the functions of nervous tissue.
B. Describe the structure of a neuron.

Nervous tissue forms the brain, spinal cord, and nerves. It is responsible for coordinating and controlling many body activities. For example, the conscious control of skeletal muscles and the unconscious regulation of cardiac muscle are accomplished by nervous tissue. Awareness of ourselves and the external environment, emotions, reasoning skills, and memory are other functions performed by nervous tissue. Many of these functions depend on the ability of nervous tissue cells to communicate with one another and with the cells of other tissues by means of electrical signals.

Nervous tissue consists of neurons and support cells, called glial cells. The **neuron** (NYUR-on), or *nerve cell,* is responsible for conducting electrical signals. It is composed of three parts: (1) a cell body, (2) dendrites, and (3) an axon (table 4.12). The **cell body** contains the nucleus and is the site of general cell functions. **Dendrites** (DEN-drights; relating to a tree) usually receive stimuli that lead to electrical changes. **Axons** (AK-sons) conduct electrical signals, which usually originate at the base of an axon where it joins the cell body and travel to the end of the axon. **Glial cells** (GLEE-al; *glia,* glue) are the support cells of the nervous system. They nourish, protect, and insulate the neurons. We consider nervous tissue in greater detail in chapter 8.

Table 4.12	Nervous Tissue

Structure:
A neuron consists of dendrites, a cell body, and a long axon; glia, or support cells, surround the neurons

Function:
Neurons transmit information in the form of action potentials, store information, and integrate and evaluate data; glia support, protect, and form specialized sheaths around axons

Location:
In the brain, spinal cord, and ganglia

4.6 TISSUE MEMBRANES

Learning Outcome *After reading this section, you should be able to*

A. List the structural and functional characteristics of mucous, serous, and synovial membranes.

A **tissue membrane** is a thin sheet or layer of tissue that covers a structure or lines a cavity. Most membranes consist of epithelium and the connective tissue on which the epithelium rests. There are four tissue membranes in the body, one external and three internal. The external tissue membrane is the **skin,** or *cutaneous* (kyu-TAY-nee-us, skin) *membrane.* It is composed of stratified squamous epithelium and dense connective tissue (see chapter 5). The three major categories of *internal tissue membranes* are (1) mucous, (2) serous, and (3) synovial membranes.

Mucous Membranes

Mucous (MYU-kus) **membranes** line cavities that open to the outside of the body, such as the digestive, respiratory, and reproductive tracts (figure 4.6*a*). Mucous membranes consist of epithelial cells, their basement membrane, and a thick layer of loose connective tissue. Some mucous membranes also contain a layer of smooth muscle cells. Many, but not all, mucous membranes contain goblet cells or multicellular mucous glands that secrete mucus. The functions of mucous membranes vary, depending on their location, but they include protection, absorption, and secretion. For example, the stratified squamous epithelium of the mucous membrane in the oral cavity (mouth) performs a protective function, whereas the simple columnar epithelium of the mucous membrane in the intestines absorbs nutrients and secretes digestive enzymes and mucus. Mucous membranes also line the nasal passages. When it becomes inflamed, we experience the "runny nose" characteristic of the common cold or an allergy.

Figure 4.6 **Internal Membranes**

(*a*) Mucous membranes line cavities that open to the outside and often contain mucous glands, which secrete mucus. (*b*) Serous membranes line cavities that do not open to the exterior, do not contain glands, but do secrete serous fluid. (*c*) Synovial membranes line the cavities that surround synovial joints.

Serous Membranes

Serous (SEER-us; producing watery secretion) **membranes** line cavities that do not open to the exterior of the body (figure 4.6*b*), such as the pericardial, pleural, and peritoneal cavities. Serous membranes consist of three components: (1) a layer of simple squamous epithelium, (2) its basement membrane, and (3) a delicate layer of loose connective tissue. Serous membranes do not contain glands, but they secrete a small amount of fluid called **serous fluid,** which lubricates the surface of the membranes. Serous membranes protect the internal organs from friction, help hold them in place, and act as a selectively permeable barrier to prevent large amounts of fluid from accumulating within the serous cavities.

Synovial Membranes

Synovial (sih-NOH-vee-al) **membranes** line the cavities of freely movable joints (figure 4.6*c*). They are made up of only connective tissue and consist of modified connective tissue cells. Synovial membranes are either continuous with the dense connective tissue of the joint capsule or separated from the capsule by areolar or adipose tissue. Synovial membranes produce **synovial fluid,** which makes the joint very slippery, thereby reducing friction and allowing smooth movement within the joint. Synovial and other connective tissue membranes are discussed in chapter 6.

4.7 TISSUE DAMAGE AND INFLAMMATION

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the process of inflammation in response to tissue damage.
B. Explain how inflammation protects the body.

Inflammation (*flamma,* flame) occurs when tissues are damaged (figure 4.7). Inflammation produces five major symptoms: (1) redness, (2) heat, (3) swelling, (4) pain, and (5) disturbance of function. Although unpleasant, the processes of inflammation are usually beneficial.

Figure 4.7 outlines the steps in inflammation.

PROCESS Figure

PROCESS Figure 4.7 **Inflammation**

Injury to an area results in release of chemical mediators, which stimulate increased blood flow and migration of white blood cells to the site of tissue damage.

Understand **Some injuries result from internal tissue damage, such as an ankle sprain. Even though there's no break in the skin, inflammation is induced and the area becomes red, painful, and swollen. The medical treatment for such an injury is RICE: rest, ice, compression, and elevation. Explain how RICE is helpful in injury recovery.**

❶ Following an injury, such as getting a splinter, substances called **chemical mediators** of inflammation are released by, or activated, in the injured tissue and adjacent blood vessels. These chemical mediators include **histamine** (HIS-tah-meen) and **prostaglandins** (PROS-tah-GLAN-dinz).

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❷ Some mediators induce dilation of blood vessels and produce redness and heat. Dilation of blood vessels is beneficial because it speeds the arrival of white blood cells and other substances important for fighting infections and repairing the injury.

❸ Chemical mediators also stimulate the pain receptors and increase the permeability of blood vessels. The increased permeability allows material such as clotting proteins and white blood cells to move out of the blood vessels and into the tissue, where they can deal directly with the injury. As proteins from the blood move into the tissue, water follows the proteins into the tissue and the tissue swells, producing **edema** (ee-DEE-mah). Edema increases the pressure in the tissue, which can also stimulate neurons and cause pain. Pain, limitation of movement resulting from edema, and tissue destruction all contribute to the disturbed function. This disturbance can be valuable because it warns the person to protect the injured structure from further damage.

Sometimes the inflammatory response lasts longer or is more intense than is desirable, and the patient is given drugs to suppress the symptoms. Antihistamines block the effects of histamine, aspirin prevents the synthesis of prostaglandins, and cortisone reduces the release of several chemical mediators that cause inflammation. Still, the inflammatory response by itself may not be enough to combat the effects of injury or fight off an infection, and the patient may require antibiotics.

Apply It 6

In some injuries, tissues are so severely damaged that cells die and blood vessels are destroyed. For injuries such as these, where do the signs of inflammation, such as redness, heat, edema, and pain, occur?

4.8 TISSUE REPAIR

Learning Outcome ***After reading this section, you should be able to***

A. Explain the major events involved in tissue repair.

Tissue repair is the substitution of viable cells for dead cells. Tissue repair can occur by regeneration or by replacement. In **regeneration,** the new cells are the same type as those that were destroyed, and normal function is usually restored. In **replacement,** a new type of tissue develops, which eventually produces a scar and causes loss of some tissue function. Most wounds heal through regeneration and replacement; which process dominates depends on the tissues involved and the nature and extent of the wound.

Skin repair is a good example of tissue repair (figure 4.8).

PROCESS Figure

PROCESS Figure 4.8 **Tissue Repair**

In the process that repairs tissue damage, a clot is first formed. Next, new epithelial tissue cells grow into the wound, followed by the formation of granulation tissue. Finally, the granulation tissue is replaced with new connective tissue.

What cellular process creates the new epidermis cells in step 2?

❶ If the edges of a wound are close together, the wound fills with blood, and a clot forms (see chapter 11). The **clot** contains the threadlike protein fibrin, which binds the edges of the wound together and stops the

bleeding. The surface of the clot dries to form a **scab,** which seals the wound and helps prevent infection.

❷ During the first week, an inflammatory response induces dilation of blood vessels, which brings blood cells and other substances to the injury area. Fibrin isolates the area and neutrophils enter the tissue from the blood. The neutrophils eventually die and can accumulate as a mixture of dead cells and fluid called **pus** (puhs). The epithelium at the edge of the wound undergoes regeneration and migrates under the scab and the epithelium is restored. After the epithelium is repaired, the scab is sloughed off (shed).

❸ The clot is replaced with **granulation tissue,** a delicate, granular-appearing connective tissue that consists of fibroblasts, collagen, and capillaries. Eventually, normal connective tissue replaces the granulation tissue.

❹ By a month, a large amount of granulation tissue is converted to a scar, which at first is bright red because numerous blood vessels are present. The scar turns from red to white as collagen accumulates and the blood vessels decrease in number.

When the wound edges are far apart, the clot may not completely close the gap, and it takes much longer for the epithelial cells to regenerate and cover the wound. With increased tissue damage, the degree of inflammation is greater, there is more cell debris for the phagocytes to remove, and the risk of infection increases. Much more granulation tissue forms, and **wound contracture,** a result of the contraction of fibroblasts in the granulation tissue, pulls the edges of the wound closer together. Although wound contracture reduces the size of the wound and speeds healing, it can lead to disfiguring and debilitating scars.

Apply It 7

Explain why it is advisable to suture large wounds.

EFFECTS

At the tissue level, age-related changes affect cells and the extracellular matrix produced by them. In general, cells divide more slowly in older people compared to younger ones. The rate of red blood cell synthesis declines in the elderly. Injuries in older people heal more slowly. For example, a fracture in an adult heals slowly, and a scar, seen in radiographs of the bone, is likely to persist throughout life.

Changes in the extracellular matrix cause connective tissues with abundant collagen, such as tendons and ligaments, to become less flexible and more fragile. Elastic connective tissues become less elastic. The reduced flexibility and elasticity of connective tissue is responsible for increased wrinkling of the skin, as well as an increased tendency for older people's bones to break.

Walls of arteries also become less elastic because of changes in collagen and elastic fibers. These changes result in increased susceptibility to rupture of arteries.

SUMMARY

4.1 Tissues and Histology

1. A tissue is a group of cells with similar structure and function, along with the extracellular substances located between the cells.
2. Histology is the study of tissues.

4.2 Epithelial Tissue

Epithelial tissue covers surfaces; it usually has a basement membrane, little extracellular material, and no blood vessels.

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Functions of Epithelia

General functions of epithelia include protecting underlying structures, acting as a barrier, permitting the passage of substances, secreting substances, and absorbing substances.

Classification of Epithelia

1. Epithelia are classified according to the number of cell layers and the shape of the cells.
2. Simple epithelium has one layer of cells, whereas stratified epithelium has more than one.
3. Pseudostratified columnar epithelium is simple epithelium that appears to have two or more cell layers.
4. Transitional epithelium is stratified epithelium that can be greatly stretched.

The Relationship Between Structure and Function of Epithelial Tissues

1. Simple epithelium is involved with diffusion, secretion, or absorption. Stratified epithelium serves a protective role. Squamous cells function in diffusion or filtration. Cuboidal or columnar cells, which contain more organelles, secrete or absorb.

2. A smooth, free surface reduces friction. Microvilli increase surface area, and cilia move materials over the cell surface.
3. Tight junctions bind adjacent cells together and form a permeability barrier.
4. Desmosomes mechanically bind cells together, and hemidesmosomes mechanically bind cells to the basement membrane.
5. Gap junctions allow intercellular communication.

Glands

1. A gland is a single cell or a multicellular structure that secretes.
2. Exocrine glands have ducts, and endocrine glands do not.

4.3 Connective Tissue

Connective tissue is distinguished by its extracellular matrix.

Functions of Connective Tissue

Connective tissues enclose and separate organs and tissues; connect tissues to one another; help support and move body parts; store compounds; cushion and insulate the body; transport substances; and protect against toxins and injury.

Cells of Connective Tissue

1. The extracellular matrix results from the activity of specialized connective tissue cells; in general, -blast cells form the matrix, -cyte cells maintain it, and -clast cells break it down. Fibroblasts form protein fibers of many connective tissues, osteoblasts form bone, and chondroblasts form cartilage.
2. Connective tissue commonly contains adipocytes, mast cells, white blood cells, macrophages, and mesenchymal cells (stem cells).

Extracellular Matrix

1. The major components of the extracellular matrix of connective tissue are protein fibers, ground substance, and fluid.
2. Protein fibers of the matrix have the following characteristics:
   - Collagen fibrils are joined to form collagen fibers. The collagen fibers resemble ropes. They are strong and flexible but resist stretching.
   - Reticular fibers are fine collagen fibers that form a branching network that supports other cells and tissues.

- Elastic fibers have a structure similar to that of a spring. After being stretched, they tend to return to their original shape.

3. Ground substance has the following major components:
   - Hyaluronic acid makes fluids slippery.
   - Proteoglycan aggregates trap water, which gives tissues the capacity to return to their original shape when compressed or deformed.
   - Adhesive molecules hold proteoglycans together and to plasma membranes.

Classification of Connective Tissue

1. Areolar connective tissue is the "packing material" of the body; it fills the spaces between organs and holds them in place.
2. Adipose tissue, or fat, stores energy. Adipose tissue also pads and protects parts of the body and acts as a thermal insulator.
3. Dense connective tissue has a matrix consisting of either densely packed collagen fibers (in tendons, ligaments, and the dermis of the skin) or densely packed elastic fibers (in elastic ligaments and the walls of arteries).
4. Reticular tissue forms a framework for lymphatic structures.
5. Cartilage provides support and is found in structures such as the disks between the vertebrae, the external ear, and the costal cartilages.
6. Bone has a mineralized matrix and forms most of the skeleton of the body.
7. Blood has a liquid matrix and is found in blood vessels.

4.4 Muscle Tissue

1. Muscle tissue is specialized to shorten, or contract.
2. The three types of muscle tissue are skeletal, cardiac, and smooth muscle.

4.5 Nervous Tissue

1. Nervous tissue is specialized to conduct action potentials (electrical signals).
2. Neurons conduct action potentials, and glia support the neurons.

4.6 Tissue Membranes

Mucous Membranes

Mucous membranes line cavities that open to the outside of the body (digestive, respiratory, and reproductive tracts). They contain glands and secrete mucus.

Serous Membranes

Serous membranes line trunk cavities that do not open to the outside of the body (pleural, pericardial, and peritoneal cavities). They do not contain mucous glands but do secrete serous fluid.

Synovial Membranes

Synovial membranes line joint cavities and secrete a lubricating fluid.

4.7 Tissue Damage and Inflammation

1. Inflammation isolates and destroys harmful agents.
2. Inflammation produces redness, heat, swelling, pain, and disturbance of function.
3. Chronic inflammation results when the agent causing injury is not removed or something else interferes with the healing process.

4.8 Tissue Repair

1. Tissue repair is the substitution of viable cells for dead cells by regeneration or fibrosis. In regeneration, stem cells, which can divide throughout life, and other dividing cells regenerate new cells of the same type as those that were destroyed. In fibrosis, the destroyed cells are replaced by different cell types, which causes scar formation.
2. Tissue repair involves clot formation, inflammation, the formation of granulation tissue, and the regeneration or fibrosis of tissues. In severe wounds, wound contracture can occur.

REMEMBERING AND UNDERSTANDING

1. Define tissue and histology.
2. In what areas of the body is epithelium located? What are four characteristics of epithelial tissue?
3. Explain how epithelial tissue is classified according to the number of cell layers and the shape of the cells. What are pseudostratified columnar and transitional epithelium?
4. What kinds of functions does a single layer of epithelium perform? A stratified layer? Give an example of each.
5. Contrast the functions performed by squamous cells with those of cuboidal or columnar cells. Give an example of each.
6. What is the function of an epithelial free surface that is smooth? of one that has microvilli? of one that has cilia?
7. Name the ways in which epithelial cells may be connected to one another, and give the function for each way.
8. Define gland. Distinguish between an exocrine and an endocrine gland.
9. Explain the differences among connective tissue cells that are termed blast, cyte, and clast cells.
10. What are the functions of connective tissues?
11. What are the major connective tissue types? How are they used to classify connective tissue?
12. Describe areolar connective tissue, and give an example.
13. How is adipose tissue different from other connective tissues? List the functions of adipose tissue.
14. Describe dense collagenous connective tissue and dense elastic connective tissue, and give two examples of each.
15. Describe the components of cartilage. Give an example of hyaline cartilage, fibrocartilage, and elastic cartilage.
16. Describe the components of bone.
17. Describe the cell types and matrix of blood, and list the functions of blood.
18. Functionally, what is unique about muscle? Which of the muscle types is under voluntary control? What tasks does each type perform?
19. Functionally, what is unique about nervous tissue? What do neurons and glia accomplish? What is the difference between an axon and a dendrite?

20. Compare mucous and serous membranes according to the type of cavity they line and their secretions. Name the serous membranes associated with the lungs, heart, and abdominopelvic organs.
21. What is the function of the inflammatory response? Name the five symptoms of inflammation, and explain how each is produced.
22. Define tissue repair. What is the difference between regeneration and fibrosis?
23. Describe the process of tissue repair when the edges of a wound are close together versus when they are far apart.
24. Describe the effect of aging on cell division and the formation of extracellular matrix.

CRITICAL THINKING

1. What types of epithelium are likely to be found lining the trachea of a heavy smoker? Predict the changes that are likely to occur after he or she has stopped smoking for 1 or 2 years.
2. The blood-brain barrier is a specialized epithelium, called endothelium, in capillaries that prevents many materials from passing from the blood into the brain. What kind of cell connections would you expect to find in the blood-brain barrier?
3. One of the functions of the pancreas is to secrete digestive enzymes that are carried by ducts to the small intestine. How many cell layers and what cell shape, cell surface, and type of cell-to-cell connections would you expect to be present in the epithelium that produces the digestive enzymes?
4. Explain the consequences
   a. if simple columnar epithelium replaced the nonkeratinized stratified squamous epithelium that lines the mouth

b. if tendons were composed of dense elastic connective tissue instead of dense collagenous connective tissue

c. if bones were made entirely of elastic cartilage

5. Some dense connective tissue has elastic fibers in addition to collagen fibers. This enables a structure to stretch and then recoil to its original shape. Examples are certain ligaments that hold together the vertebrae (bones of the back). When the back is bent (flexed), the ligaments are stretched. How does the elastic nature of these ligaments help the back function? How are the fibers in the ligaments organized?
6. The aorta is a large blood vessel attached to the heart. When the heart beats, blood is ejected into the aorta, which expands to accept the blood. The wall of the aorta is constructed with dense connective tissue that has elastic fibers. How do you think the fibers are arranged?
7. Antihistamines block the effect of a chemical mediator, histamine, which is released during the inflammatory response. When could taking an antihistamine be harmful, and when could it be beneficial?

Answers to odd-numbered critical thinking questions from this chapter appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

5

Integumentary System

The integumentary system includes the skin and accessory structures, such as hair, glands, and nails.

LEARN TO APPLY IT

Mia, Christine, and Landon are so excited about spending the day together. Their mothers are happy to see the children playing outside and getting some exercise. They spend the whole day running through the waves and playing in the sun. At the end of the day, Mia and Landon have tanned a bit, but poor Christine has sunburn, a condition that affects the integumentary system.

By applying the information you learn from this chapter, explain what natural and artificial factors may have influenced the children's different reactions to the day of sun exposure.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 4 Integumentary System

5.1 FUNCTIONS OF THE INTEGUMENTARY SYSTEM

Learning Outcome ***After reading this section, you should be able to***

A. Describe the general functions of the integumentary system.

The **integumentary** (in-teg-you-MEN-tah-ree) **system** consists of the skin and accessory structures, such as hair, glands, and nails. Integument means covering, and the integumentary system is one of the more familiar systems of the body to everyone because it covers the outside of the body and is easily observed. We are also familiar with this system because we are concerned with the appearance of the integumentary system. Skin without blemishes is considered attractive, whereas acne is a source of embarrassment for many teenagers. The development of wrinkles and the graying or loss of hair are signs of aging. We invest much time, effort, and money on altering and enhancing the appearance of the integumentary system. Many of us apply lotion to our skin, color our hair, and trim our nails. We also try to prevent sweating by using antiperspirants and to reduce or mask body odor by washing and by using deodorants and perfumes.

The appearance of the integumentary system can indicate physiological imbalances in the body. Some disorders, such as acne or warts, affect just the integumentary system. Other disorders affect different parts of the

body but are reflected in the integumentary system, providing useful signs for diagnosis. For example, reduced blood flow through the skin during a heart attack can cause a person to look pale, whereas increased blood flow as a result of increased body temperature can cause a flushed appearance. Also, some diseases cause skin rashes, such as those characteristic of measles, chicken pox, and allergic reactions. In addition, the integumentary system and the other systems often interact in complex ways in both healthy and diseased states (see Systems Pathology, "Burns," later in this chapter).

Although we are often concerned with how the integumentary system looks, it has many important functions that go beyond appearance. Major functions of the integumentary system include.

1. *Protection*. The skin provides protection against abrasion and ultraviolet light. It also prevents microorganisms from entering the body and reduces water loss, thus preventing dehydration.
2. *Sensation*. The integumentary system has sensory receptors that can detect heat, cold, touch, pressure, and pain.
3. *Vitamin D production*. When exposed to ultraviolet light, the skin produces a molecule that can be transformed into vitamin D, an important regulator of calcium homeostasis.
4. *Temperature regulation*. The amount of blood flow beneath the skin's surface and the activity of sweat glands in the skin both help regulate body temperature.
5. *Excretion*. Small amounts of waste products are lost through the skin and in gland secretions.

5.2 SKIN

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the structure and function of the epidermis.
B. Explain the process of keratinization.
C. Describe the epidermal strata.
D. Describe the structure and discuss the function of the dermis.
E. Explain how melanin, blood, carotene, and collagen affect skin color.

The skin is made up of two major tissue layers: (1) the epidermis and (2) the dermis. The **epidermis** (ep-ih-DER-miss; upon the dermis) is the

most superficial layer of skin. It is a layer of epithelial tissue that rests on the **dermis** (DER-miss), which is a layer of dense connective tissue (figure 5.1). The thickness of the epidermis and dermis varies, depending on location, but on average the dermis is 10 to 20 times thicker than the epidermis. The epidermis provides protection. The dermis is responsible for most of the skin's structural strength. The skin rests on the **subcutaneous** (sub-kew-TAY-nee-us; under the skin) **tissue,** which is also a layer of connective tissue. The subcutaneous tissue is not part of the skin, but it does connect the skin to underlying muscle or bone. To give an analogy, if the subcutaneous tissue is the foundation on which a house rests, the dermis forms most of the house and the epidermis is its roof.

Figure 5.1 **Skin and Subcutaneous Tissue**

The skin, consisting of the epidermis and the dermis, is connected by the subcutaneous tissue to underlying structures. Note the accessory structures (hairs, glands, and arrector pili), some of which project into the subcutaneous tissue, and the large amount of adipose tissue in the subcutaneous tissue.

Epidermis

The epidermis is stratified squamous epithelium; in its deepest layers, new cells are produced by mitosis. As new cells form, they push older cells to the surface, where they slough, or flake off. The many cells of the epidermis prevent water loss and resist abrasion. The outermost cells protect the cells underneath, and the deeper, replicating cells replace cells lost from the surface. During their movement, the cells change shape and chemical composition, a process called **keratinization** (KER-ah-tin-i-ZAY-shun). The term keratinization reflects the fact that the cells become filled with the protein **keratin** (KER-ah-tin), which makes them more rigid and durable. As keratinization proceeds, epithelial cells eventually die and form an outer layer of dead, rigid cells that resists abrasion and acts as a permeability barrier.

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Although keratinization is a continuous process, distinct cellular characteristics can be recognized. These characteristics are used to divide the epidermis into layers called **strata** (STRAH-tah; layers). From the deepest to the most superficial, the five strata are the (1) strata basale, (2) stratum spinosum, (3) stratum granulosum, (4) stratum lucidum, and (5) stratum corneum (figure 5.2). The **stratum basale** (ba-SAL-eh; a base) consists of cuboidal or columnar cells that undergo mitotic divisions about every 19 days. One daughter cell becomes a new stratum basale cell and can divide again. The other daughter cell is pushed toward the surface, a journey that takes about 40–56 days. As cells move to the surface, changes in the cells produce intermediate strata (see figure 5.2*b*). Cells of the **stratum spinosum** (spi-NO-sum) take on a flattened appearance and accumulate lipid-filled vesicles called lamellar bodies. Cells of the **stratum granulosum** (gran-you-LO-sum) are flat and diamond shaped. The cells accumulate more keratin and release the contents of the lamellar bodies to the extracellular space. The cells' nuclei and organelles degenerate, and the cells die, giving this layer its characteristic grainy appearance.

Figure 5.2 APR **Epidermis and Dermis**

(a) The epidermis rests on the dermis. Dermal papillae project toward the epidermis. *(b)* As skin cells move from one stratum to the next, they undergo a series of changes called keratinization. The five epidermal strata, from deep to superficial, are (1) stratum basale, (2) stratum spinosum, (3) stratum granulosum, (4) stratum lucidum, and (5) stratum corneum.

The **stratum lucidum** (LOO-see-dum) is a thin, clear zone between the stratum granulosum and stratum corneum. The stratum lucidum is

present in certain areas of the body. The cells of this stratum no longer have nuclei or organelles, and as a result, the cells stain more lightly. Skin is classified as thick or thin based on the structure of the epidermis. **Thick skin** has all five strata and is found in areas subject to pressure or friction, such as the palms of the hands, the soles of the feet, and the fingertips. **Thin skin** lacks the stratum lucidum and covers the rest of the body. The terms thick skin and thin skin only refer to the number of epidermal strata and not to the overall thickness of the skin, which is determined by the dermis.

The **stratum corneum** (COR-nee-um) is the most superficial stratum of the epidermis. It consists of dead squamous cells filled with keratin. Keratin gives the stratum corneum its structural strength. The stratum corneum cells are also coated and surrounded by lipids released from the lamellar bodies of the skin cells. These lipids act as waterproofing material, thereby preventing fluid loss through the skin.

Apply It 1

What kinds of substances could easily pass through the skin by diffusion? What kinds would have difficulty?

The stratum corneum is composed of 25 or more layers of dead squamous cells joined by desmosomes (see chapter 4). Eventually, the desmosomes break apart, and the cells are sloughed from the skin. Excessive sloughing of stratum corneum cells from the surface of the scalp is called dandruff. In skin subjected to friction, the number of layers in the stratum corneum greatly increases, producing a thickened area called a **callus** (KAL-us; hard skin). Over a bony prominence, the stratum corneum can thicken to form a cone-shaped structure called a **corn.**

Dermis

The dermis is composed of dense collagenous connective tissue containing fibroblasts, adipocytes, and macrophages. Nerves, hair follicles, smooth muscles, glands, and lymphatic vessels extend into the dermis (see figure 5.1).

Collagen and elastic fibers are responsible for the strength of the dermis. The collagen fibers of the dermis are oriented in many different directions

and can resist stretch. However, more collagen fibers are oriented in some directions than in others. This produces **cleavage lines,** or *tension lines,* in the skin, and the skin is most resistant to stretch along these lines (figure 5.3). It is important for surgeons to be aware of cleavage lines. An incision made across the cleavage lines is likely to gap and produce considerable scar tissue, but an incision made parallel with the lines tends to gap less and produce less scar tissue (see chapter 4).

Figure 5.3 **Cleavage Lines**

The orientation of collagen fibers produces cleavage lines, or tension lines, in the skin.

If the skin is overstretched for any reason, the dermis can be damaged, leaving lines that are visible through the epidermis. These lines, called **stretch marks,** can develop when a person increases in size quite rapidly. For example, stretch marks often form on the skin of the abdomen and

breasts of a female during pregnancy or on the skin of athletes who have quickly increased muscle size by intense weight training.

The upper part of the dermis has projections called **dermal papillae** (pah-PILL-ee; nipple), which extend toward the epidermis (see figure 5.2). Recall that the epidermis lacks blood vessels; however, the dermal papillae contain many blood vessels. Blood flow through these vessels supplies the overlying epidermis with nutrients, removes waste products, and helps regulate body temperature. The dermal papillae in the palms of the hands, the soles of the feet, and the tips of the digits are arranged in parallel, curving ridges that shape the overlying epidermis into patterns called **friction ridges.** The impressions left on surfaces by these friction ridges are fingerprints and footprints. As the name suggests, the ridges increase friction and improve the grip of the hands and feet.

An injection delivers substances, such as medicines, to the body by puncturing the skin. Substances are administered at different depths in the skin, depending on how quickly the material needs to enter the blood. An **intradermal injection** delivers material to the blood slowly and is administered by drawing the skin taut and inserting a small needle at a shallow angle into the dermis; an example is the tuberculin skin test. A **subcutaneous injection** is achieved by pinching the skin to form a "tent" and inserting a short needle into the adipose tissue of the subcutaneous tissue; an example is an insulin injection. An **intramuscular injection** delivers material to the blood faster than intradermal or subcutaneous injections. An intramuscular injection is accomplished by inserting a long needle at a 90-degree angle to the skin into a muscle deep to the subcutaneous tissue. Intramuscular injections are used for most vaccines and certain antibiotics.

Skin Color

Several factors determine skin color: (1) pigments in the skin, (2) blood circulating through the skin, and (3) the thickness of the stratum corneum. **Melanin** (MEL-ah-nin; black) is the group of pigments primarily responsible for skin, hair, and eye color. Most melanin molecules are brown to black pigments, but some are yellowish or reddish. Melanin provides protection against ultraviolet light from the sun.

Melanin is produced by **melanocytes** (MEL-an-oh-cytes; melano, black + kytos, cell). Melanocytes are irregularly shaped cells located between the stratum basale and the stratum spinosum. They have many long processes that extend between the epithelial cells of the deep part of the epidermis.

Figure 5.4 illustrates the process of melanin transfer from melanocytes to epithelial cells.

PROCESS Figure

PROCESS Figure 5.4 APR **Melanin Transfer to Epithelial Cells**
Melanocytes make melanin, which is packaged into melanosomes and transferred to many epithelial cells.

Melanin protects a cell's DNA from UV damage. Based on this information, around which cellular structure would you expect the melanosomes to congregate?

❶ Within melanocytes, the Golgi apparatuses package melanin into vesicles called **melanosomes** (MEL-ah-no-sohms).

❷ Melanosomes move into the cell processes of the melanocytes.

❸ Epithelial cells phagocytize the tips of the melanocyte cell processes, thereby acquiring melanosomes. Although all the epithelial cells of the epidermis can contain melanin, only the melanocytes produce it.

Large amounts of melanin form freckles or moles in some regions of the skin, as well as darkened areas in the genitalia, the nipples, and the circular

areas around the nipples. Other areas, such as the lips, palms of the hands, and soles of the feet, contain less melanin.

Melanin production is determined by genetic factors, exposure to light, and hormones. Genetic factors are responsible for the amounts of melanin produced resulting in variation in skin color in the human population. Since all humans have about the same number of melanocytes, skin color variations are determined by the amount, kind, and distribution of melanin. Although many genes are responsible for skin color, a single mutation can prevent the production of melanin. For example, **albinism** (AL-bi-niz-em) is a recessive genetic trait that causes a deficiency or an absence of melanin, resulting in fair skin, white hair, and unpigmented irises in the eyes.

CLINICAL IMPACT

Skin Cancer

Skin cancer is the most common type of cancer. Although chemicals and radiation (x-rays) are known to induce cancer, the development of skin cancer most often is associated with exposure to ultraviolet (UV) light from the sun. Consequently, most skin cancers develop on the face, neck, or hands. The group of people most likely to have skin cancer is fair-skinned (they have less protection from the sun) or older than 50 (they have had long exposure to the sun).

There are three main types of skin cancer. **Basal cell carcinoma** (kar-sih-NOH-mah), the most frequent type, begins with cells in the stratum basale and extends into the dermis to produce an open ulcer (figure 5.5*a*). Surgical removal or radiation therapy cures this type of cancer. Fortunately, there is little danger that this type of cancer will spread, or metastasize, to other areas of the body. **Squamous cell carcinoma** develops from cells immediately superficial to the stratum basale. Normally, these cells undergo little or no cell division, but in squamous cell carcinoma, the cells continue to divide as they produce keratin. The typical result is a nodular, keratinized tumor confined to the epidermis (figure 5.5*b*). If untreated, the tumor can invade the dermis, metastasize, and cause death. **Malignant melanoma** (MEL-ah-NOH-mah) is a rare form of skin cancer that arises from melanocytes, usually in a preexisting mole. A mole is an aggregation, or "nest," of melanocytes. The melanoma can appear as a large, flat, spreading lesion or as a

deeply pigmented nodule (figure 5.5*c*). Metastasis is common, and unless diagnosed and treated early in development, this cancer is often fatal.

Figure 5.5 **Cancer of the Skin**

(*a*) Basal cell carcinoma. (*b*) Squamous cell carcinoma. (*c*) Malignant melanoma.

(a) Dr. P. Marazzi/Science Photo Library/Getty Images; (b) Dr. P. Marazzi/Science Source; (c) © National Cancer Institute

Limiting exposure to the sun and using sunscreens that block ultraviolet light can reduce the likelihood of developing skin cancer. Ultraviolet light is classified into two types based on their wavelengths: UVA has a longer wavelength than UVB. Exposure to UVA causes most tanning of the skin but is associated with the development of malignant melanoma. Exposure to UVB causes most burning of the skin and is associated with the development of basal cell and squamous cell carcinomas. It is advisable to use sunscreens that effectively block both UVA and UVB. This information will be useful as you answer the Learn to Apply It question at the beginning of this chapter.

Exposure to ultraviolet light—for example, in sunlight—stimulates melanocytes to increase melanin production. The result is a suntan. The production of melanin in response to ultraviolet light is a protective measure, reducing DNA damage in the cell. How does this information relate to the Learn to Apply It question at the beginning of this chapter?

Certain hormones, such as estrogen and melanocyte-stimulating hormone, cause an increase in melanin production during pregnancy in the mother, darkening the nipples, the pigmented circular areas around the nipples, and the genitalia even more. The cheekbones and forehead can also darken, resulting in “the mask of pregnancy.” Also, a dark line of pigmentation can appear on the midline of the abdomen.

Blood flowing through the skin imparts a reddish hue, and when blood flow increases, the red color intensifies. Examples include blushing and the redness resulting from the inflammatory response. A decrease in blood flow, as occurs in shock, can make the skin appear pale. A decrease in the blood O_2 content produces a bluish color of the skin, called **cyanosis**

(sigh-ah-NOH-sis; dark blue). Birthmarks are congenital (present at birth) disorders of the blood vessels in the dermis.

Carotene (KAIR-oh-teen) is a yellow pigment found in plants such as squash and carrots. Humans normally ingest carotene and use it as a source of vitamin A. Carotene is lipid-soluble, and when consumed it accumulates in the lipids of the stratum corneum and in the adipocytes of the dermis and subcutaneous tissue. If large amounts of carotene are consumed, the skin can become quite yellowish.

The location of pigments and other substances in the skin affects the color produced. If a dark pigment is located in the dermis or subcutaneous tissue, light reflected off the dark pigment can be scattered by collagen fibers of the dermis to produce a blue color. The deeper within the dermis or subcutaneous tissue any dark pigment is located, the bluer the pigment appears because of the light-scattering effect of the overlying tissue. This effect causes the blue color of tattoos, bruises, and some superficial blood vessels.

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Apply It 2

Explain the differences in skin color between (a) the palms of the hands and the lips, (b) the palms of the hands of a person who does heavy manual labor and one who does not, and (c) the anterior and posterior surfaces of the forearm.

5.3 SUBCUTANEOUS TISSUE

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the structure of the subcutaneous tissue.
B. Discuss the function of the subcutaneous tissue.

Just as a house rests on a foundation, the skin rests on the **subcutaneous tissue,** or *hypodermis* (high-poh-DER-miss; under the dermis). The subcutaneous tissue is not part of the skin but instead attaches the skin to underlying bone and muscle and supplies it with blood vessels and nerves (see figure 5.1). The subcutaneous tissue is loose connective tissue, including adipose tissue that contains about half the body's stored lipids. The amount and location of adipose tissue vary with age, sex, and diet.

Adipose tissue in the subcutaneous tissue functions as padding and insulation, and it is responsible for some of the differences in appearance between males and females as well as between individuals of the same sex.

The subcutaneous tissue can be used to estimate total body fat. The skin and subcutaneous tissue are pinched at selected locations, and the thickness of the fold is measured. The thicker the fold, the greater the amount of total body fat. The percentage of body fat varies in the population, but on average females have higher total body fat than do males. The acceptable percentage of body fat varies from 21% to 30% for females and from 13% to 25% for males. A body fat percentage above the acceptable range is an indicator of obesity.

5.4 ACCESSORY SKIN STRUCTURES

Learning Outcomes *After reading this section, you should be able to*

A. Describe the structure of a hair.
B. Discuss the phases of hair growth.
C. Name the glands of the skin, and describe the secretions they produce.
D. Describe the parts of a nail.
E. Explain how nails grow.

Accessory structures of the skin are attached to or embedded into the skin. The accessory skin structures are hair, glands, and nails.

Hair

In humans, **hair** is found everywhere on the skin, except on the palms, the soles, the lips, the nipples, parts of the genitalia, and the distal segments of the fingers and toes.

Each hair arises from a **hair follicle,** an invagination of the epidermis that extends deep into the dermis (figure 5.6*a*). A helpful analogy for the structure of the hair follicle and hair is a single flower in a vase. The vase is like the hair follicle and the flower stem is like the hair. The **shaft** of the hair protrudes above the surface of the skin, whereas the **root** is below the surface. The **hair bulb** is the expanded base of the root.

Figure 5.6 APR **Hair Follicle**

(*a*) Hair within a hair follicle. (*b*) Enlargement of the hair bulb and hair follicle wall. The hair bulb is the expanded base of the hair root (see the regions of the hair around the hair papilla).

MICROBES IN YOUR BODY

Acne: Using Bacteria to Fight Bacteria

Acne (ak′ ne) is the most common skin condition in the United States, affecting both adolescents and adults. Acne is inflammation of the hair follicles and sebaceous glands. Lesions of acne are caused by the overproduction of epidermal cells in the hair follicle. These excess cells are shed from the hair follicle wall and mix with sebum secreted by sebaceous glands of the hair follicle. The combination of sebum and dead cells forms a blockage in the hair follicle. Sebum accumulates behind the blockage producing a "whitehead." A "blackhead" develops when the accumulating mass of cells and sebum push through the hair follicle opening. If the wall of the hair follicle ruptures, bacteria can enter the tissue, causing an infection and inflammation. This results in the formation of a pimple.

Four factors are believed to be responsible for acne: (1) hormones, (2) sebum, (3) abnormal production of cells, and (4) the bacterium *Propionibacterium acnes (P. ancnes)*. There is no tried-and-true cure for acne; however, new research examining the skin microbiome may have found a natural and effective treatment for maintaining healthy, clear skin. Different strains of the bacterium *P. acnes* are found in the sebum-rich areas of the skin, such as the forehead, side of the nose, and back. Although it has been difficult to study these bacteria, the inception of the Human Genome Project (see "Getting to Know Your Bacteria" in chapter 1) allowed scientists to determine the specific genetic traits of skin microbiome bacteria. Using this technique, scientists have identified three unique strains of *P. acnes*. Of the three strains, one strain in more dominant in people with acne-free skin. Research has shown that this strain of *P. acnes* does not adversely affect the skin. Let's call this one the "good" *P. acnes*. However, the other two strains of *P. acnes are* pathogenic to humans. We will refer to these as the "bad" *P. acnes*.

So, how does this information help scientists learn how to prevent acne? It seems that the "good" *P. acnes* prevents invasion of the skin by certain bacteria, including the "bad" *P. acnes*, through a natural metabolic process. When *P. acnes* breaks down lipids, the skin pH is lowered to a level not tolerated by the invading bacteria. Because acne-affected people do not host the "good" strain, on their skin the "bad" strain can increase in population and cause annoying acne eruptions. Perhaps in the future, to prevent acne, affected people can apply the "good" *P. acnes* in a cream to prevent the "bad" *P. acnes* from taking over.

A hair has a hard **cortex,** which surrounds a softer center, the **medulla** (meh-DULL-ah). The cortex is covered by the **cuticle** (KEW-tih-cul; skin), a single layer of overlapping cells that holds the hair in the hair follicle. Because the hair follicle is composed of epithelial tissue, hair follicles can play an important role in repair of the skin. If the surface epidermis is

damaged, the epithelial cells within the hair follicle can divide and serve as a source of new epithelial cells.

Hair is produced in the hair bulb, which rests on the hair papilla (figure 5.6*b*). The **hair papilla** is an extension of the dermis that protrudes into the hair bulb. Blood vessels within the papilla supply the hair bulb with the nourishment needed to produce the hair.

Hair is produced in cycles of growth and rest. During the growth stage, a hair is formed by epithelial cells within the hair bulb. These cells, like the cells of the stratum basale in the skin, divide and undergo keratinization. The hair grows longer as these cells are added to the base of the hair within the hair bulb. Thus, the hair root and shaft consist of columns of dead keratinized epithelial cells.

During the resting stage, growth stops and the hair is held in the hair follicle. When the next growth stage begins, a new hair is formed and the old hair falls out.

The duration of each stage depends on the individual hair. Eyelashes grow for about 30 days and rest for 105 days, whereas scalp hairs grow for 3 years and rest for 1–2 years. The loss of hair normally means that the hair is being replaced because the old hair falls out of the hair follicle when the new hair begins to grow. In some individuals, however, a permanent loss of hair results in "pattern baldness." Although many of the hair follicles are lost, some remain and produce a very short, transparent hair, which for practical purposes is invisible. These changes occur when male sex hormones act on the hair follicles of individuals who have the genetic predisposition for pattern baldness.

Hair color is determined by varying amounts and types of melanin. The production and distribution of melanin by melanocytes occurs in the hair bulb by the same method as in the skin. With age, the amount of melanin in hair can decrease, causing the hair color to become faded, or the hair can contain no melanin and be white. Gray hair is usually a mixture of unfaded, faded, and white hairs.

Apply It 3

Marie Antoinette's hair supposedly turned white overnight after she heard she would be sent to the guillotine. Explain why you believe or disbelieve this story.

Associated with each hair follicle are smooth muscle cells called the **arrector** (ah-REK-tor; that which raises) **pili** (PIE-lee; hair) (see figure

5.6*a*). Contraction of the arrector pili causes the hair to become more perpendicular to the skin's surface, or to "stand on end," and it produces a raised area of skin called a "goose bump."

Glands

The major glands of the skin are the **sebaceous** (se-BAY-shus) **glands** and the **sweat glands** (figure 5.7). Sebaceous glands are simple, branched acinar glands (see chapter 4). Most are connected by a duct to the superficial part of a hair follicle. They produce **sebum,** an oily, white substance rich in lipids. The sebum is released by holocrine secretion (see chapter 4) and lubricates the hair and the surface of the skin, which prevents drying and protects against some bacteria.

Figure 5.7 **Glands of the Skin**
Sebaceous glands and apocrine sweat glands empty into a hair follicle. Eccrine sweat glands empty onto the surface of the skin.

There are two kinds of sweat glands: (1) eccrine and (2) apocrine. **Eccrine** (EK-rin) **sweat glands** are simple, coiled, tubular glands and release sweat by merocrine secretion. Eccrine glands are located in almost

every part of the skin but most numerous in the palms and soles. They produce a secretion that is mostly water with a few salts. Eccrine sweat glands have ducts that open onto the surface of the skin through sweat pores. When the body temperature starts to rise above normal levels, the sweat glands produce sweat, which evaporates and cools the body. Emotional sweating can also occur in the palms, soles, armpits, and other places.

Apocrine (AP-oh-krin) **sweat glands** are simple, coiled, tubular glands that produce a thick secretion rich in organic substances. These substances are released primarily by merocrine secretion, though some glands demonstrate holocrine secretion. They open into hair follicles, but only in the armpits and genitalia. Apocrine sweat glands become active at puberty because of the influence of reproductive hormones. The organic secretion, which is essentially odorless when released, is quickly broken down by bacteria into substances responsible for what is commonly known as body odor.

Nails

The **nail** is a thin plate, consisting of layers of dead stratum corneum cells that contain a very hard type of keratin. The visible part of the nail is the **nail body,** and the part of the nail covered by skin is the **nail root** (figure 5.8). The **cuticle,** or *eponychium* (ep-oh-NIK-ee-um), is stratum corneum that extends onto the nail body. The nail root extends distally from the **nail matrix.** The nail also attaches to the underlying **nail bed,** which is located distal to the nail matrix. The nail matrix and bed are epithelial tissue with a stratum basale that gives rise to the cells that form the nail. The nail matrix is thicker than the nail bed and produces most of the nail. A small part of the nail matrix, the **lunula** (LOO-noo-lah; moon), can be seen through the nail body as a whitish, crescent-shaped area at the base of the nail. Cell production within the nail matrix causes the nail to grow. Unlike hair, nails grow continuously and do not have a resting stage.

Figure 5.8 APR **Nail**

(*a*) Dorsal view of the exterior nail. (*b*) Lateral view of a sagittal section through the nail. Most of the epidermis is absent from the nail bed.

5.5 PHYSIOLOGY OF THE INTEGUMENTARY SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Discuss the role of skin, hair, glands, and nails in protection.
B. List the various sensations detected by structures of the integumentary system.
C. Discuss the process of vitamin D production in the body.
D. Discuss the importance of the skin in temperature regulation.
E. Describe the role of the skin in excretion.

Protection

The integumentary system performs many protective functions.

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1. The intact skin plays an important role in reducing water loss because its lipids act as a barrier to the diffusion of water from the deeper tissues of the body to the surface of the epidermis.
2. The skin acts as a barrier that prevents microorganisms and other foreign substances from entering the body. Secretions from skin glands also produce an environment unsuitable for some microorganisms.
3. The stratified squamous epithelium of the skin protects underlying structures against abrasion.
4. Melanin absorbs ultraviolet light and protects underlying structures from its damaging effects.
5. Hair provides protection in several ways: The hair on the head acts as a heat insulator, eyebrows keep sweat out of the eyes, eyelashes protect the eyes from foreign objects, and hair in the nose and ears prevents the entry of dust and other materials.
6. The nails protect the ends of the fingers and toes from damage.

Sensation

Many sensory receptors are associated with the skin. Receptors in the epidermis and dermis can detect pain, heat, cold, and pressure (see chapter 9). Although hair does not have a nerve supply, sensory receptors around the hair follicle can detect the movement of a hair.

Vitamin D Production

When the skin is exposed to ultraviolet light, a precursor molecule of **vitamin D** is formed. The precursor is carried by the blood to the liver, where it is modified, and then to the kidneys, where the precursor is modified further to form active vitamin D. Take a moment to develop a flow diagram illustrating the steps involved in the production of active vitamin D, highlighting the specific areas of the body involved.

If exposed to enough ultraviolet light, humans can produce all the vitamin D they need. However, many people need to ingest vitamin D as well because clothing and indoor living reduce their exposure to ultraviolet light. Fatty fish (and fish oils) and vitamin D–fortified milk are the best sources of vitamin D. Eggs, butter, and liver contain small amounts of vitamin D but are not considered significant sources because too large a serving size is necessary to meet the daily vitamin D requirement. Adequate levels of vitamin D are necessary because active vitamin D stimulates the small intestine to absorb calcium and phosphate, the substances necessary for normal bone growth (see chapter 6) and normal muscle function (see chapter 7).

Temperature Regulation

Body temperature normally is maintained at about 37°C (98.6°F). Recall from chapter 1 that homeostatic control mechanisms maintain a relatively constant internal environment, including body temperature (see figure 1.5). Regulation of body temperature is important because the rate of chemical reactions within the body can be increased or decreased by changes in body temperature. Even slight changes in temperature can make enzymes operate less efficiently and disrupt the normal rates of chemical changes in the body.

Exercise, fever, and an increase in environmental temperature tend to raise body temperature. In order to maintain homeostasis, the body must rid itself of excess heat. Figure 5.9 illustrates the heat exchange at the skin.

PROCESS Figure

PROCESS Figure 5.9 APR Heat Exchange in the Skin

Blood transfers heat from deeper tissues to the surface of the skin, where the heat is lost. Alteration of blood vessel diameter, and therefore blood flow, allows for regulation of heat loss at the skin.

Explain why placing an ice pack on the skin results in that area of the skin appearing red.

1. Blood vessels in the dermis dilate and enable more blood to flow within the skin, thus transferring heat from deeper tissues to the skin.
2. The excess heat is lost by radiation (infrared energy), convection (air movement), or conduction (direct contact with an object). Excess heat is also released as sweat spreads over the surface of the skin and evaporates, thus reducing body temperature.
3. Heat can be conserved by the constriction of dermal blood vessels, which reduces blood flow to the skin.
4. Thus, less heat is transferred from deeper structures to the skin, and heat loss is reduced.

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When we are exposed to cold environments, blood vessels in the dermis constrict and smaller amounts of warm blood flow through the skin, causing a decrease in skin temperature. If the skin temperature drops below about 15°C (59°F), dermal blood vessels dilate.

Apply It 4

You may have noticed that when you exercise, your face turns red. Can you explain the advantage of this response? How is this different from when your nose and ears turn red on cold days?

Excretion

The integumentary system plays a minor role in **excretion,** the removal of waste products from the body. In addition to water and salts, sweat contains small amounts of waste products, such as urea, uric acid, and ammonia. Even though the body can lose large amounts of sweat, the sweat glands do not play a significant role in the excretion of waste products.

5.6 INTEGUMENTARY SYSTEM AS A DIAGNOSTIC AID

Learning Outcome *After reading this section, you should be able to*

A. Explain how the integumentary system can be used as a diagnostic aid.

The integumentary system is useful in diagnosis because it is observed easily and often reflects events occurring in other parts of the body. Can you think of three "illnesses" that are indicated by changes in the skin? Here are a few examples. Cyanosis, a bluish color to the skin caused by decreased blood O_2 content, is an indication of impaired circulatory or respiratory function. A yellowish skin color, called **jaundice** (JAWN-dis), can occur when the liver is damaged by a disease, such as viral hepatitis. Normally, the liver secretes bile pigments, breakdown products of worn-out red blood cells, into the small intestine. Bile pigments are yellow, and their buildup in the blood and tissues can indicate impaired liver function.

Rashes and lesions in the skin can be symptoms of problems elsewhere in the body. For example, scarlet fever results when bacteria infecting the throat release a toxin into the blood that causes a reddish rash on the skin. The development of a rash can also indicate an allergic reaction to foods or to drugs, such as penicillin.

The condition of the skin, hair, and nails is affected by nutritional status. In vitamin A deficiency, the skin produces excess keratin and assumes a characteristic sandpaper texture, whereas in iron-deficiency anemia the nails lose their normal contour and become flat or concave (spoon-shaped).

Hair concentrates many substances that can be detected by laboratory analysis, and a patient's hair can be compared with a "normal" hair for certain diagnoses. For example, lead poisoning results in high levels of lead in the hair. However, the use of hair analysis to determine the general health or nutritional status of an individual is unreliable.

5.7 BURNS

Learning Outcome *After reading this section, you should be able to*

A. Classify burns on the basis of the amount of skin damage produced.

A **burn** is injury to a tissue caused by heat, cold, friction, chemicals, electricity, or radiation. Burns are classified according to their depth (figure 5.10). In **partial-thickness burns,** part of the stratum basale remains viable, and regeneration of the epidermis occurs from within the burn area,

as well as from the edges of the burn. Partial-thickness burns are divided into first- and second-degree burns.

Figure 5.10 **Burns**

Burns are classified based on the extent of skin damage. Partial-thickness burns are subdivided into first-degree burns (damage to only the epidermis) and second-degree burns (damage to the epidermis and part of the dermis). Full-thickness, or third-degree, burns destroy the epidermis, the dermis, and sometimes deeper tissues.

First-degree burns involve only the epidermis and are red and painful. Slight **edema** (ee-DEE-mah), or swelling, may be present. They can be caused by sunburn or brief exposure to very hot or very cold objects, and they heal without scarring in about a week.

Second-degree burns damage both the epidermis and the dermis. If dermal damage is minimal, symptoms include redness, pain, edema, and blisters. Healing takes about 2 weeks, and no scarring results. However, if the burn goes deep into the dermis, the wound appears red, tan, or white; can take several months to heal; and might scar. In all second-degree burns, the epidermis, including the stratum basale where the stem cells are found, is damaged. As a result, the epidermis regenerates from epithelial tissue in hair follicles and sweat glands, as well as from the edges of the wound.

In **full-thickness burns,** or *third-degree burns*, the epidermis and the dermis are completely destroyed, and recovery occurs from the edges of the burn wound. Third-degree burns often are surrounded by areas of first- and second-degree burns. Although the first- and second-degree burn areas are painful, the region of third-degree burn is usually painless because sensory receptors in the epidermis and dermis have been destroyed. Third-degree burns appear white, tan, brown, black, or deep cherry red.

SYSTEMS PATHOLOGY

Burns

Background Information

Sam is a 23-year-old male who fell asleep while smoking. His burning cigarette started a fire. Burns can damage the body in many ways (figure 5.11). Sam received partial-thickness and full-thickness burns to his face, arms, upper torso, and legs (figure 5.12). When large areas of skin are severely burned, the resulting systemic effects can be life-threatening. Within minutes of a major burn injury, there is increased permeability of small blood vessels called capillaries. This increased permeability occurs at the burn site and throughout the body. As a result, fluid and ions are lost from the burn wound and into tissue spaces. The loss of fluid decreases blood volume, which decreases the heart's ability to pump blood. The resulting decrease in blood delivery to tissues can cause tissue damage, shock, and even death. Treatment consists of administering intravenous fluid at a faster rate than it leaks out of the capillaries. Although this fluid replacement can reverse the shock and prevent death, fluid continues to leak into tissue spaces, causing pronounced edema (swelling). Typically, after 24 hours, capillary permeability returns to normal, and the amount of intravenous fluid administered can be greatly decreased.

Figure 5.11 Systems Interactions: Burns

Burns affect more than just the skin. This diagram illustrates how the systems of the body are affected following a burn.

Figure 5.12 Degrees of Burn

Full-thickness and partial-thickness burns

James Stevenson/Science Photo Library/Science source

Substances released from the burn may also play a role in causing cells to function abnormally. Burn injuries result in an almost immediate hypermetabolic state, resulting from an increase in body temperature and changes in hormone secretion. Compared with a normal body temperature of approximately 37°C (98.6°F), a typical

burn patient may have a body temperature of 38.5°C (101.3°F), despite the higher loss of water by evaporation from the burn.

In severe burns, the increased metabolic rate can result in loss of as much as 30–40% of the patient's preburn weight. To help compensate, treatment may include doubling or tripling the patient's caloric intake. In addition, the need for protein, which is necessary for tissue repair, is greater.

Normal skin maintains homeostasis by preventing microorganisms from entering the body. Because burns damage and sometimes completely destroy the skin, microorganisms can cause infections. For this reason, burn patients are maintained in an aseptic (sterile) environment (figure 5.13), which attempts to prevent the entry of microorganisms into the wound. They are also given antimicrobial drugs, which kill microorganisms or suppress their growth. **Debridement** (dah-BREED-ment), the removal of dead tissue from the burn, helps prevent infections by cleaning the wound and removing tissue in which infections could develop. Skin grafts, performed within a week of the injury, also help close the wound and prevent the entry of microorganisms.

Figure 5.13 Treatment in Sterile Environment

Patient in a burn unit

Stan Levy/Science Source

Despite these efforts, however, infections are still the major cause of death for burn victims. Depression of the immune system during the first or second week after the injury contributes to the high infection rate. First, the thermally altered tissue is recognized as a foreign substance, which stimulates the immune system. Then, the immune system is overwhelmed as immune system cells become less effective and the production of the chemicals that normally provide resistance to infections decreases (see chapter 14). The greater the magnitude of the burn, the greater the depression of the immune system, and the greater the risk of infection.

TABLE 5.1 REPRESENTATIVE DISEASES AND DISORDERS: Skin

Condition	Description
Ringworm	Fungal infection that produces patchy scaling and inflammatory response in the skin
Eczema and dermatitis	Inflammatory conditions of the skin caused by allergy, infection, poor circulation, or exposure to chemical or environmental factors

Condition	Description
Psoriasis	Chronic skin disease characterized by thicker than normal epidermal layer (stratum corneum) that sloughs to produce large, silvery scales; bleeding may occur if the scales are scraped away
Bacterial Infections	
Impetigo	Small blisters containing pus; easily rupture to form a thick, yellowish crust; usually affects children
Decubitus ulcers (bedsores or pressure sores)	Develop in people who are bedridden or confined to a wheelchair; compression of tissue and reduced circulation result in destruction of the subcutaneous tissue and skin, which later become infected by bacteria, forming ulcers
Viral Infections	
Rubeola (measles)	Skin lesions; caused by a virus contracted through the respiratory tract; may develop into pneumonia or infect the brain, causing damage
Rubella (German measles)	Skin lesions; usually mild viral disease contracted through the respiratory tract; may be dangerous if contracted during pregnancy because the virus can cross the placenta and damage the fetus
Chicken pox	Skin lesions; usually mild viral disease contracted through the respiratory tract
Shingles	Painful skin lesions that can recur when the dormant virus is activated by trauma, stress, or another illness; caused by the chicken pox virus after childhood infection
Cold sores (fever blisters)	Skin lesions; caused by herpes simplex I virus; transmitted by oral or respiratory routes; lesions recur
Genital herpes	Genital lesions; caused by herpes simplex II virus; transmitted by sexual contact

Venous thrombosis (throm-BOH-sis), the development of a clot in a vein, is another complication of burns. Blood normally forms a clot when exposed to damaged tissue, such as at a burn site, but clotting can also occur elsewhere, such as in veins, where clots can block blood flow, resulting in tissue destruction. The concentration of chemicals that cause blood clotting (called clotting factors) increases for two reasons: Loss of fluid from the burn patient concentrates the chemicals, and the liver releases an increased amount of clotting factors.

Apply It 5

When Sam was first admitted to the burn unit, the nurses carefully monitored his urine output. Why does that make sense in light of his injuries?

MENTARY SYSTEM

As the body ages, the skin is more easily damaged because the epidermis thins and the amount of collagen in the dermis decreases. Skin infections are more likely, and repair of the skin occurs more slowly. The skin begins to sag and wrinkle because of a decrease in the number of elastic fibers in the dermis and loss of adipose tissue from the subcutaneous tissue. A decrease in the activity of sweat glands and in the blood supply to the dermis results in reduced ability to regulate body temperature. The skin becomes drier as sebaceous gland activity decreases. The number of melanocytes generally decreases, but in some areas the number of melanocytes increases to produce **age spots.** Note that age spots are different from **freckles,** which are caused by increased melanin production. Gray or white hair also results because of a decrease in or a lack of melanin production. Skin that is exposed to sunlight shows signs of aging more rapidly than nonexposed skin, so avoiding overexposure to sunlight and using sunscreen is advisable.

Fourth-degree burns are extremely severe burns that affect tissues deeper than the subcutaneous tissue. These burns often damage muscle, bone, and other tissues associated with them. Like third-degree burns, fourth-degree burns are painless due to the destruction of the pain receptors. Because these burns are so severe, amputation or complete

removal of the damaged tissue is required. Resultant increased susceptibility to infection can cause death.

Deep partial-thickness and full-thickness burns take a long time to heal, and they form scar tissue with disfiguring and debilitating wound contracture (see chapter 4). To prevent these complications and to speed healing, skin grafts are often performed. In a procedure called a split skin graft, the epidermis and part of the dermis are removed from another part of the body and placed over the burn. Interstitial fluid from the burn nourishes the graft until blood vessels can grow into the graft and supply it with nutrients. Meanwhile, the donor tissue produces new epidermis from epithelial tissue in the hair follicles and sweat glands in the same manner as in superficial second-degree burns.

When it is not possible or practical to move skin from one part of the body to a burn site, physicians sometimes use artificial skin or grafts from human cadavers. However, these techniques are often unsatisfactory because the body's immune system recognizes the graft as a foreign substance and rejects it. A solution to this problem is to grow some of the burn victim's own skin in the laboratory. A piece of healthy skin from the burn victim is removed and placed in a flask with nutrients and hormones that stimulate rapid growth. The new skin that results consists only of epidermis and does not contain glands or hair.

SUMMARY

The integumentary system consists of the skin, hair, glands, and nails.

5.1 Functions of the Integumentary System

The integumentary system consists of the skin, hair, glands, and nails. The integumentary system protects us from the external environment. Other functions include sensation, vitamin D production, temperature regulation, and excretion of small amounts of waste products.

5.2 Skin

Epidermis

1. The epidermis is stratified squamous epithelium divided into strata.
   - Strata from deep to superficial are stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum.
   - New cells are produced in the stratum basale.
   - The stratum corneum consists of many layers of dead squamous cells containing keratin. The most superficial layers are sloughed.
2. Keratinization is the transformation of stratum basale cells into stratum corneum cells.
   - Structural strength results from keratin inside the cells and from desmosomes, which hold the cells together.
   - Lipids surrounding the stratum corneum cells help prevent fluid loss.

Dermis

1. The dermis is dense connective tissue.
2. Collagen and elastic fibers provide structural strength, and the blood vessels of the papillae supply the epidermis with nutrients.

Skin Color

1. Melanocytes produce melanin, which is responsible for different skin colors. Melanin production is determined genetically but can be modified by exposure to ultraviolet light and by hormones.
2. Carotene, a plant pigment ingested as a source of vitamin A, can cause the skin to appear yellowish.
3. Increased blood flow produces a red skin color, whereas decreased blood flow causes a pale skin color. Decreased blood O_2 results in the blue skin color of cyanosis.
4. Scattering of light by collagen produces a bluish color.

5.3 Subcutaneous Tissue

1. The subcutaneous tissue, which is not part of the skin, is loose connective tissue that attaches the skin to underlying tissues.
2. About half of the body's lipids are stored in the subcutaneous tissue.

5.4 Accessory Skin Structures

Hair

1. Hairs are columns of dead, keratinized epithelial cells. Each hair consists of a shaft (above the skin), a root (below the skin), and a hair bulb (site of hair cell formation).
2. Hairs have a growth phase and a resting phase.
3. Contraction of the arrector pili, which are smooth muscles, causes hair to "stand on end" and produces a "goose bump."

Glands

1. Sebaceous glands produce sebum, which oils the hair and the surface of the skin.
2. Eccrine sweat glands produce sweat, which cools the body.
3. Apocrine sweat glands produce an organic secretion that causes body odor when broken down by bacteria.

Nails

1. The nail consists of the nail body and the nail root.
2. The nail matrix produces the nail, which is composed of stratum corneum cells containing hard keratin.

5.5 Physiology of the Integumentary System

Protection

The skin reduces water loss, prevents the entry of microorganisms, and provides protection against abrasion and ultraviolet light; hair and nails also perform protective functions.

Sensation

The skin contains sensory receptors for pain, heat, cold, and pressure.

Vitamin D Production

1. Ultraviolet light stimulates the production of a precursor molecule in the skin that is modified by the liver and kidneys into vitamin D.

2. Vitamin D increases calcium uptake in the small intestine.

Temperature Regulation

1. Through dilation and constriction of blood vessels, the skin controls heat loss from the body.
2. Evaporation of sweat cools the body.

Excretion

Skin glands remove small amounts of waste products but are not important in excretion.

5.6 Integumentary System as a Diagnostic Aid

The integumentary system is easily observed and often reflects events occurring in other parts of the body (e.g., cyanosis, jaundice, rashes).

5.7 Burns

1. Partial-thickness burns damage only the epidermis (first-degree burn) or the epidermis and the dermis (second-degree burn).
2. Full-thickness burns (third-degree burns) destroy the epidermis, the dermis, and usually underlying tissues.
3. Fourth-degree burns damage tissue deeper than the subcutaneous tissue, including muscle and bone.

REME MBER ING AND UNDE

RSTA NDIN G

1. Name the components of the integumentary system.
2. What kind of tissue is the epidermis? In which stratum of the epidermis are new cells formed? From which stratum are they sloughed?
3. Define keratinization. What structural changes does keratinization produce to make the skin resistant to abrasion and water loss?
4. What type of tissue is the dermis? What is responsible for its structural strength? How does the dermis supply the epidermis with blood?
5. Name the cells that produce melanin. What happens to the melanin after it is produced? What is the function of melanin?
6. Describe the factors that determine the amount of melanin produced in the skin.
7. How do melanin, blood, carotene, and collagen affect skin color?
8. What type of tissue is the subcutaneous tissue, and what are its functions?
9. What is a hair follicle? Define the root, shaft, and hair bulb of a hair. What kinds of cells are found in a hair?
10. Why is a hair follicle important in the repair of skin?
11. What part of a hair is the site of hair growth? What are the stages of hair growth?
12. What happens when the arrector pili of the skin contract?
13. What secretion do the sebaceous glands produce? What is the function of the secretion?
14. Which glands of the skin are responsible for cooling the body? Which glands are involved in producing body odor?
15. Name the parts of a nail. Where are the cells that make up the nail produced, and what kind of cells make up a nail? What is the lunula? Describe nail growth.
16. How do the components of the integumentary system provide protection?

17. List the types of sensations detected by receptors in the skin.
18. Describe the production of vitamin D by the body. What is the function of vitamin D?
19. How does the integumentary system help regulate body temperature?
20. Name the substances excreted by skin glands. Is the skin an important site of excretion?
21. Why is the skin a useful diagnostic aid? Give three examples of how the skin functions as a diagnostic aid.
22. Define the different categories of burns. How is repair accomplished after each type?

CRITICAL THINKING

1. A woman has stretch marks on her abdomen, yet she states that she has never been pregnant. Is this possible? Explain your conclusion.
2. It has been several weeks since Tom has competed in a tennis match. After the match, he discovers that a blister has formed beneath an old callus on his foot and the callus has fallen off. When he examines the callus, it appears yellow. Can you explain why?
3. The lips are muscular folds forming the anterior boundary of the oral cavity. A mucous membrane covers the lips internally, and the skin of the face covers them externally. The red part of the lips (called the vermillion border) is covered by keratinized epithelium that is a transition between the epithelium of the mucous membrane and the facial skin. The vermillion border can become chapped (dry and cracked), whereas the mucous

membrane and the facial skin do not. Propose as many reasons as you can to explain why the vermillion border is more prone to drying than the mucous membrane or the facial skin.

4. Pulling on hair can be quite painful, but cutting hair is not painful. Explain.
5. Given what you know about the cause of acne, propose some ways to prevent or treat it.
6. Consider the following statement: Dark-skinned children are more susceptible to rickets (insufficient calcium in the bones) than light-skinned children. Defend or refute this statement.
7. Harry, a light-skinned man, jogs on a cool day. What color would you expect his skin to be (a) after going outside and just before starting to run, (b) during the run, and (c) 5 minutes after the run?

Answers to odd-numbered critical thinking questions from this chapter appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

6

Skeletal System: Bones and Joints

The skeletal system is the framework that helps maintain the body's shape and enables us to move normally. The skeletal system is composed of bones, cartilage, and ligaments.

Biophoto Associates/Science Source

LEARN TO APPLY IT

Dr. Thomas Miller and Dr. Roberta Rogers had worked together for almost two decades, and Dr. Rogers knew something was bothering Dr. Miller. She noticed him wincing in pain whenever he bent down to retrieve something from a bottom shelf, and he was short-tempered rather than his usual happy self. Dr. Rogers knew that Dr. Miller would never admit to being injured if it meant he couldn't care for his patients, even if only for a few days. Finally, Dr. Rogers convinced him to let her x-ray his lower back. Right away, when Dr. Rogers showed Dr. Miller the x-ray, he pointed to the cause of the pain he'd been suffering.

Remember **Based on your knowledge of vertebral column anatomy, in what region is his injury located?**

Understand **Why is this region of the vertebral column more prone to this type of injury than other regions?**

Answers to these questions and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Anatomy & Physiology Revealed 4.0

Module 5 Skeletal System

6.1 FUNCTIONS OF THE SKELETAL SYSTEM

Learning Outcome ***After reading this section, you should be able to***

A. Explain the functions of the skeletal system.

Sitting, standing, walking, picking up a pencil, and taking a breath all involve the skeletal system. Without the skeletal system, there would be no rigid framework to support the soft tissues of the body and no system of joints and levers to allow the body to move. The skeletal system consists of bones as well as their associated connective tissues, including cartilage, tendons, and ligaments. These are all dynamic, living tissues that are able to grow, detect pain stimuli, adapt to stress, and undergo repair after injury.

The skeleton is usually thought of as the framework of the body, but the skeletal system has many other functions as well, including the following:

1. *Body support.* Rigid, strong bone is well suited for bearing weight and is the major supporting tissue of the body. Cartilage provides firm yet flexible support within certain structures, such as the nose, external ear, thoracic cage, and trachea. **Ligaments**, strong bands of fibrous connective tissue, hold bones together.
2. *Organ protection.* Bone is hard and protects the organs it surrounds. For example, the skull encloses and protects the brain, and the vertebrae surround the spinal cord. The rib cage protects the heart, lungs, and other organs of the thorax.

3. *Body movement.* Skeletal muscles attach to bones by tendons, which are strong bands of connective tissue. Contraction of the skeletal muscles moves the bones, producing body movement. Joints, which are formed where two or more bones come together, allow movement between bones. Ligaments allow some movement between bones but prevent excessive movement.
4. *Mineral storage.* Some minerals in the blood are stored in bone. If blood levels of these minerals decrease, the minerals are released from bone into the blood. The principal minerals stored are calcium and phosphorous, two minerals essential for many physiological processes. Adipose tissue is also stored within bone cavities. If needed, the lipids are released into the blood and used by other tissues as a source of energy.
5. *Blood cell production.* Many bones contain cavities filled with red bone marrow, which produces blood cells and platelets (see chapter 11).

6.2 BONE HISTOLOGY

Learning Outcomes *After reading this section, you should be able to*

A. Describe the components of the extracellular matrix, and explain the function of each.
B. List each type of bone cell.
C. Give the function of each type of bone cell.
D. Explain the structural differences between compact bone and spongy bone.

In chapter 4 you learned that cartilage, tendons, ligaments, and bones are all types of connective tissue. Recall that connective tissue is characterized by having widely distributed cells separated by a nonliving material called matrix. In these structures of the skeletal system, the cells produce the matrix and become entrapped within it. The cells also break down old matrix so that new matrix can replace it. The composition of each tissue's matrix is responsible for its characteristics. For example, the fibrous protein **collagen** provides flexibility but resists pulling or compression. This makes collagen well-adapted for the attachment functions of tendons and ligaments as well as the shock absorption of cartilage. In addition, recall from chapter 4 that the matrix ground substance consists of molecules called **proteoglycans,** water-trapping proteins, which helps cartilage be smooth and resilient.

Bone Matrix

By weight, mature bone matrix is normally about 35% organic and 65% inorganic material. The organic material consists primarily of collagen and proteoglycans. The inorganic material consists primarily of a calcium phosphate crystal called **hydroxyapatite** (hye-DROK-see-ap-ah-tyte), which has the molecular formula $Ca_{10}(PO_4)_6(OH)_2$. The collagen and mineral components are responsible for the major functional characteristics of bone. Bone matrix can be compared to reinforced concrete. Like reinforcing steel bars, the collagen fibers lend flexible strength to the matrix; like concrete, the mineral components give the matrix weight-bearing

strength. If mineral in a long bone is reduced, collagen becomes the primary constituent and the bone is overly flexible. On the other hand, if the amount of collagen is reduced in the bone, the mineral component becomes the primary constituent and the bone is very brittle.

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Brittle bone disease, or osteogenesis imperfecta, which means imperfect bone formation, is a rare disorder caused by any one of a number of faulty genes that results in either too little collagen formation, or poor quality collagen. As a result, the bone matrix has decreased flexibility and is more easily broken than normal bone.

Apply It 1

What would a bone be like if the majority of the minerals were removed? What would it be like if the majority of the collagen were removed?

Bone Cells

There are three types of bone cells—(1) osteoblasts, (2) osteocytes, and (3) osteoclasts—each with different functions and a unique origin.

Osteoblasts

Osteoblasts (OS-tee-oh-blasts) are bone-building cells. These cells have an extensive endoplasmic reticulum and numerous ribosomes. Osteoblasts produce collagen and proteoglycans, which are packaged into vesicles by the Golgi apparatus and secreted by exocytosis. Osteoblasts also secrete high concentrations of Ca2+ and phosphate ions, forming crystals called hydroxyapatite. The hydroxyapatite crystals act as templates that stimulate further hydroxyapatite formation and mineralization of the matrix. The formation of new bone by osteoblasts is called **ossification** (OS-ih-fih-KAY-shun), or *osteogenesis* (OS-tee-oh-JEN-eh-sis). Ossification can occur multiple times during life: as a fetus, when growing larger, and any time in life when a fracture is repaired. Ossification occurs by appositional growth on the surface of previously existing material, either bone or cartilage. For example, osteoblasts beneath the periosteum cover the surface of preexisting bone. Bone matrix produced by the osteoblasts covers the older bone surface and surrounds the osteoblast cell bodies and extensions. The result is a new layer of bone.

Osteocytes

Osteoblasts become **osteocytes** (OS-tee-oh-sites) once the osteoblasts have secreted sufficient bone matrix (figure 6.1*a*). Osteocytes account for 90–95% of bone cells and are very long-lived, with a life span of up to 25 years. Osteocytes can produce the components needed to maintain the bone matrix.

Figure 6.1 **Osteoblasts, Osteocytes, and Osteoclasts**

(*a*) Osteoblasts produce bone matrix until they become surrounded by bone matrix, after which they are called osteocytes. (*b*) Osteocytes are housed in pits called lacunae that have cell extensions in canaliculi. (*c*) Osteoclasts are massive, multinucleated cells that secrete acid and protein-digesting enzymes that degrade bone. These cells then transport the digested matrix from the bone into the blood.

Biophoto Associates/Science Source

Osteocyte cell bodies are housed within the bone matrix in spaces called **lacunae** (la-KOO-nee). Osteocyte cell extensions are housed in narrow, long spaces called

canaliculi (kan-ah-LIK-yoo-lie; little canals; figure 6.2*b*). In a sense, the cells and their extensions form a "mold" around which the matrix is formed. Nutrients and gases can pass through the small amount of fluid surrounding the cells in the canaliculi and lacunae or pass from cell to cell.

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Figure 6.2 APR **Spongy Bone**
(*a*) Beams of bone, the trabeculae, surround spaces in the bone. In life, the spaces are filled with red or yellow bone marrow and with blood vessels. (*b*) Transverse section of a trabecula.

Osteoclasts

Osteoclasts (OS-tee-oh-klasts) are bone-destroying cells (figure 6.1*b*). These cells break down bone. Breakdown of bone is called bone reabsorption. This breakdown is important for mobilizing crucial Ca^{2+} and phosphate ions for use in many metabolic processes. Note that we use the term *reabsorption* here because our point of reference is the bloodstream. As bone is broken down, the Ca^{2+} goes "back" into the blood. Osteoclasts are massive, multinucleated cells and develop from the red bone marrow cells that also differentiate into specialized white blood cells.

Mature osteoclasts carry out bone reabsorption through a multistep process. First, the osteoclasts must access the bone matrix. Once the osteoclasts have come in contact with the bone surface, the osteoclasts form attachment structures, which create a sealed compartment under the osteoclast. Next, the osteoclasts develop a **ruffled border** (figure 6.1*c*).

The ruffled border is a specialized reabsorption-specific area of the membrane. Osteoclasts create an acidic environment within the sealed compartment, which causes breakdown of the bone matrix. Enzymes are secreted into the sealed compartment, where they digest the organic, protein component of the bone matrix. After breakdown of the matrix, the degradation products are secreted into the blood and used elsewhere in the body.

Spongy and Compact Bone

As bone forms, the newly formed bone goes through several stages. Recall that ossification can occur throughout your lifetime. Mature bone is called **lamellar bone.** It is organized into thin, concentric sheets or layers, called **lamellae** (lah-MEL-ee). In general, the collagen fibers of one lamella lie parallel to one another, but at an angle to the collagen fibers in the adjacent lamellae. Osteocytes, within their lacunae, are arranged in layers sandwiched between lamellae.

As ossification continues, bone is further molded and shaped into its final form. Bone can be classified according to the amount of bone matrix relative to the amount of space within the bone. Spongy bone, which appears porous, has less bone matrix and more space than compact bone. In contrast, compact bone has more bone matrix and less space than spongy bone. **Spongy bone** consists of interconnecting rods or plates of bone called **trabeculae** (trah-BEK-yoo-lee; beam; figure 6.2*a*). Between the trabeculae are spaces, which in life are filled with bone marrow and blood vessels. Most trabeculae are thin and consist of several lamellae, with osteocytes located in lacunae between the lamellae (figure 6.2*b*). Each osteocyte is associated with other osteocytes through canaliculi. Usually no blood vessels penetrate the trabeculae, so osteocytes must obtain nutrients through their canaliculi. The surfaces of trabeculae are covered with a single layer of cells consisting mostly of osteoblasts with a few osteoclasts.

Compact bone, or *cortical bone,* is the solid, outer layer surrounding each bone. It has more matrix and is denser with fewer pores than spongy bone (figure 6.3). Blood vessels enter the substance of the bone itself, and the lamellae of compact bone are primarily oriented around those blood vessels. The functional unit of compact bone is an **osteon** (OS-tee-on), or haversian (hah-VER-shan) system. An osteon is composed of concentric rings of matrix, which surround a central tunnel and contain osteocytes. In cross section, an osteon resembles a circular target; the bull's-eye of the target is the **central canal.** Surrounding the central canal are rings of bone matrix. Central canals are lined with endosteum and contain blood vessels, nerves, and loose connective tissue. Blood vessels are contained within the central canals. Osteocytes are located in lacunae between the lamellar rings, and canaliculi

radiate between lacunae across the lamellae, looking like minute cracks across the rings of the target.

Figure 6.3 APR **Structure of Bone Tissue**

(*a*) Compact bone consists mainly of osteons, which are lamellae surrounding blood vessels within central canals. The outer surface of the bone is also formed by lamellae. (*b*) Photomicrograph of an osteon. (*c*) An individual osteon showing lamellae, lacunae, and canaliculi.

(a) ©Trent Stephens; (b) Biophoto Associates/Science Source

Canals running from the periosteum or medullary cavity also contain blood vessels (figure 6.3*a*). Nutrients in the blood vessels are delivered to the osteocytes. Because the osteocytes are in contact with each other through the canaliculi, nutrients are passed from one osteocyte to another osteocyte within each osteon. Waste products are removed in the reverse direction.

6.3 BONE ANATOMY

Learning Outcome ***After reading this section, you should be able to***

A. Label the parts of a typical long bone.

Structure of a Long Bone

A long bone is the traditional model for overall bone structure (figure 6.4). The **diaphysis** (die-AF-ih-sis) is the center portion of the bone. It is composed primarily of compact bone tissue, surrounding a hollow center called the **medullary cavity.** Some spongy bone tissue can be found lining the medullary cavity. The ends of a long bone are called **epiphyses** (e-PIF-ih-seez; sing. -sis). The epiphyses are mostly spongy bone, with an outer layer of compact bone. Within joints, the end of a long bone is covered with hyaline cartilage called **articular cartilage** (figure 6.4*a,b*). The **epiphyseal** (ep-i-FEEZ-ee-al) **plate,** or *growth plate*, is located between the epiphysis and the diaphysis (figure 6.4*a*). Growth in bone length (discussed in section 6.5) occurs at the epiphyseal plate. Consequently, growth in length of the long bones of the arm, forearm, thigh, and leg occurs at both ends of the diaphysis, whereas growth in length of the hand and foot bones occurs at one end of the diaphysis. When bone stops growing in length, the epiphyseal plate becomes ossified and is called the **epiphyseal line** (figure 6.4*b*).

Figure 6.4 **Structure of a Long Bone**

The femur (thighbone) serves as a model of the parts of a long bone. (*a*) The presence of epiphyseal plates, as well as the condition of the diaphysis and epiphyses, shows that this is a young bone. (*b*) Adult long bone with epiphyseal lines. (*c*) Internal features of a portion of the diaphysis in (*a*).

(a) ©Trent Stephens

The cavities of spongy bone and the medullary cavity are filled with marrow. **Red marrow** is the site of blood cell formation, and **yellow marrow** is mostly adipose tissue. In the fetus, the spaces within bones are filled with red marrow. The conversion of red marrow to yellow marrow begins just before birth and continues well into adulthood. Yellow marrow completely replaces the red marrow in the long bones of the limbs, except for some red marrow in the proximal part of the arm bones and thighbones. The hipbone is used as a source of donated red bone marrow

because it is a large bone with more red bone marrow than smaller bones and it can be accessed relatively easily.

The **periosteum** (PER-ee-OSS-tee-um) is a connective tissue membrane covering the outer surface of a bone (figure 6.4*c*). The outer layer contains blood vessels and nerves, whereas the inner layer is a single layer of bone cells, including osteoblasts and osteoclasts (see section 6.2). Where tendons and ligaments attach to bone, the collagen fibers of the tendon or ligament become continuous with those of the periosteum. In addition, some of the collagen fibers of the tendons or ligaments penetrate the periosteum into the outer part of the bone and strengthen the attachment of the tendons or ligaments to the bone.

The **endosteum** (en-DOSS-tee-um) is a single cell layer of connective tissue that lines the internal surfaces of all cavities within bones, such as the medullary cavity of the diaphysis and the smaller cavities in spongy and compact bone (figure 6.4*c*). The endosteum includes osteoblasts and osteoclasts.

6.4 BONE DEVELOPMENT

Learning Outcomes *After reading this section, you should be able to*

A. Outline the process of intramembranous ossification.
B. Describe the steps of endochondral ossification.
C. List the bones, or parts of bones, that develop from each type of ossification.

Bone formation in the fetus follows two processes: (1) **intramembranous ossification** and (2) **endochondral ossification.**Intramembranous ossification starts within embryonic connective tissue membranes. Endochondral ossification starts with a cartilage model.

Intramembranous Ossification

Many skull bones, part of the mandible (lower jaw), and the diaphyses of the clavicles (collarbones) develop by intramembranous ossification (figure 6.5). At approximately the fifth week of development in an embryo, a membrane of connective tissue with delicate, randomly oriented collagen fibers surrounds the brain. This membrane will eventually become cranial bones of the skull. Intramembranous ossification of this membrane begins at approximately the eighth week of embryonic development and is completed by approximately 2 years of age. The locations in the membrane where intramembranous ossification begins are called **centers of ossification.** The centers of ossification expand to form a bone by gradually ossifying the membrane. Thus, the centers have the oldest bone, and the expanding edges the youngest bone. **Fontanels,** or soft spots, are the larger, membrane-covered spaces between the developing skull bones that have not yet been ossified (figure 6.5; see section 6.12). The bones eventually grow together, and all the fontanels have usually closed by 2 years of age. Figure 6.5 shows the steps in intramembranous ossification.

PROCESS Figure

PROCESS Figure 6.5 **Intramembranous Ossification and Bone Formation in a Fetus**

(a) This panel shows the skull of a 12-week-old fetus. In this figure, bones formed by intramembranous ossification are in yellow and include the frontal bone and parietal bone, and bones formed by endochondral ossification are blue and include the ethmoid bone, sphenoid bone, and the inferior portion of the occipital bone. Intramembranous ossification starts at a center of ossification and expands outward. Therefore, the youngest bone is at the edge of the expanding bone and the

oldest bone is at the center of ossification. Steps 1–3 show progressively older bone as the skull develops. (*b*) Radiograph of an 18-week-old fetus, showing intramembranous and endochondral ossification. Intramembranous ossification occurs at ossification centers in the flat bones of the skull. Endochondral ossification has formed bones in the diaphyses of long bones. The epiphyses are still cartilage at this stage of development.

(a) (top, bottom): ©Victor Eroschenko; (middle): Ed Reschke/Getty Images; (b) Biophoto Associates/Science Source

What type of cellular process is most likely the mechanism employed by osteoblasts to release bone matrix until they are surrounded by it?

❶ *Osteoblast activity*: Osteoblasts within the center of ossification begin producing bone matrix. The bone matrix will surround the collagen fibers of the existing connective tissue membrane. Once the osteoblasts are embedded in bone matrix, the osteoblasts become osteocytes. As a result of this process, many tiny trabeculae of woven bone develop.

❷ *Spongy bone formation*: Additional osteoblasts gather on the surfaces of the trabeculae and produce more bone, thereby causing the trabeculae to become larger and longer. Spongy bone forms as the trabeculae join together.

❸ *Compact bone formation*: Cells within the spaces of the spongy bone specialize to form red bone marrow, and cells surrounding the developing bone specialize to form the periosteum. Osteoblasts from the periosteum lay down bone matrix to form an outer surface of compact bone.

Thus, the end products of intramembranous bone formation are bones with outer compact bone surfaces and spongy centers (see figure 6.2).

Endochondral Ossification

The formation of cartilage begins at approximately the end of the fourth week of embryonic development. Endochondral ossification of some of this cartilage starts at approximately the eighth week of embryonic development, but this process might not begin in other cartilage until as late as 18–20 years of age. Bones of the base of the skull, part of the mandible, the epiphyses of the clavicles, and most of the remaining skeletal system develop through endochondral ossification (figure 6.5). Figure 6.6 outlines the steps in endochondral ossification

PROCESS Figure

PROCESS Figure 6.6 Endochondral Ossification of a Long Bone

Endochondral ossification begins with the formation of a hyaline cartilage model. It begins in the diaphysis with a primary ossification center and progresses to the epiphyses with secondary ossification centers.

What type of cellular process is most likely the mechanism employed by osteoclasts to remove the calcified cartilage in the ossification centers?

1. *Cartilage model formation*: A hyaline **cartilage model** is produced by cells called **chondrocytes** (KON-droh-sites), and has the approximate shape of the future bone. The cartilage model is surrounded by perichondrium.
2. *Bone collar formation*: Once osteoblasts begin to produce bone, the perichondrium becomes the periosteum. The osteoblasts produce compact bone on the surface of the cartilage model, forming a **bone collar.** Two other events occur at the same time as the bone collar is forming. First, the cartilage model increases in size as a result of interstitial and appositional cartilage growth. Interstitial growth occurs as a result of continuous cell division of the chondrocytes within the cartilage model. Appositional growth occurs as a result of cell division at the surface of the cartilage model, and under the perichondrium. Second, the chondrocytes in the center of the cartilage model absorb some of the cartilage matrix and **hypertrophy** (high-PER-troh-fee), or enlarge. The chondrocytes also initiate the formation of hydroxyapatite crystals in the cartilage matrix. At this point, the cartilage is called **calcified cartilage.** The chondrocytes in this calcified area eventually die, leaving enlarged lacunae with thin walls of calcified matrix.
3. *Primary ossification center formation*: Blood vessels grow into the enlarged lacunae of the calcified cartilage. Osteoblasts and osteoclasts migrate into the calcified cartilage area from the periosteum by way of the connective tissue surrounding the outside of the blood vessels. The **primary ossification center**

forms as osteoblasts produce bone on the surface of the calcified cartilage. The osteoblasts transform the calcified cartilage of the diaphysis into spongy bone.

As bone development proceeds, the cartilage model continues to grow, the bone collar thickens. Osteoclasts remove bone from the center of the diaphysis to form the medullary cavity, and cells within the medullary cavity specialize to form red bone marrow.

4. *Secondary ossification center formation*: **Secondary ossification centers** are created in the epiphyses by osteoblasts that migrate into the epiphysis. The events occurring at the secondary ossification centers are the same as those at the primary ossification centers, except that the spaces in the epiphyses do not enlarge to form a medullary cavity as in the diaphysis.

   Replacement of cartilage by bone continues in the cartilage model until all the cartilage, except that in the epiphyseal plate and on articular surfaces, has been replaced by bone. The epiphyseal plate, which exists during the time a person's bones are actively growing, and the articular cartilage, which is a permanent structure, are derived from the original embryonic cartilage model. After a person's bones have stopped growing, the epiphyseal plate regresses into a "scar," called the epiphyseal line (see section 6.5).

5. *Adult bone*: In mature bone, spongy and compact bone are fully developed, and the epiphyseal plate has become the epiphyseal line. The only cartilage present is the articular cartilage at the ends of the bone. All the original perichondrium that surrounded the cartilage model has become periosteum.

6.5 BONE GROWTH

Learning Outcome *After reading this section, you should be able to*

A. Demonstrate an understanding of bone growth in length and width.

Unlike cartilage, bones do not grow by interstitial growth only. Bones increase in size in part by appositional growth, the formation of new bone on the surface of older bone or cartilage. For example, trabeculae grow in size when osteoblasts deposit new bone matrix onto the surface of the trabeculae (see figure 6.5).

Growth in Bone Length

Long bones increase in length because of growth at the epiphyseal plate. In a long bone, the epiphyseal plate separates the epiphysis from the diaphysis (figure 6.7*a*).

PROCESS Figure

PROCESS Figure 6.7 **Endochondral Bone Growth**

(*a*) Radiograph and drawing of the knee, showing the epiphyseal plate of the tibia (shinbone). Because cartilage does not appear readily on x-ray film, the epiphyseal plate appears as a black area between the white diaphysis and the epiphyses. (*b*) Zones of the epiphyseal plate, including newly ossified bone. (*c*) New cartilage forms on the epiphyseal side of the plate at the same rate as new bone forms on the diaphyseal side of the plate. Consequently, the epiphyseal plate remains the same thickness but the diaphysis increases in length.

(a) Ed Reschke/Photolibrary/Getty Images; (c) Biophoto Associates/Science Source

Apply

Growth hormone is the principal hormone controlling bone growth during childhood. Given the process of endochondral bone growth, how do you think growth hormone stimulates growth in height?

Long bones grow by creating new cartilage in the epiphyseal plate. Cartilage calcification and ossification in the epiphyseal plate occur by the same basic process as calcification and ossification of the cartilage model during endochondral bone

formation. New cartilage forms through interstitial cartilage growth followed by appositional bone growth on the surface of the existing cartilage. The epiphyseal plate is organized into five zones (figure 6.7*b, c*).

❶ The zone of resting cartilage is nearest the epiphysis and contains slowly dividing chondrocytes.

❷ The chondrocytes in the zone of proliferation produce new cartilage by dividing and forming columns resembling stacks of plates or coins.

❸ In the zone of hypertrophy, the chondrocytes produced in the zone of proliferation mature and enlarge.

❹ The zone of calcification is very thin and contains hypertrophied chondrocytes and calcified cartilage matrix. The hypertrophied chondrocytes die, and blood vessels from the diaphysis grow into the area. The connective tissue surrounding the blood vessels contains osteoblasts from the endosteum.

❺ The osteoblasts line up on the surface of the calcified cartilage and deposit new bone matrix, which is later remodeled.

As new cartilage cells form in the zone of proliferation, and as these cells enlarge in the zone of hypertrophy, the overall length of the diaphysis increases (figure 6.7b, *c*). However, the thickness of the epiphyseal plate does not increase, because the rate of cartilage growth on the epiphyseal side of the plate is equal to the rate of bone formation on the diaphyseal side of the plate.

As the bones achieve normal adult size, they stop growing in length because the epiphyseal plate has ossified and become the epiphyseal line. This event, called closure of the epiphyseal plate, occurs between approximately 12 and 25 years of age, depending on the bone and the individual.

Apply It 2

Describe the appearance of an adult if cartilage growth did not occur in the long bones during childhood.

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6.6 BONE REMODELING

Learning Outcome *After reading this section, you should be able to*

A. Explain the need for bone remodeling, particularly in long bones.

Just as our homes must be remodeled when they fall into disrepair, bone that becomes old is replaced with new bone in a process called **bone remodeling.** In this process, osteoclasts remove old bone and osteoblasts deposit new bone. Bone remodeling converts woven bone into lamellar bone and is involved in several

important functions, including bone growth, changes in bone shape, adjustment of the bone to stress, bone repair, and calcium ion (Ca^{2+}) regulation in the body.

The structure of a long bone—a hollow cylinder with a medullary cavity in the center—has two mechanical advantages: (1) A hollow cylinder is lighter in weight than a solid rod, and (2) a hollow cylinder with the same height, weight, and composition as a solid rod, but with a greater diameter, can support much more weight without bending. As a long bone increases in length and diameter, the size of the medullary cavity also increases, keeping the bone from becoming very heavy. In addition, as the bone grows in diameter, the relative thickness of compact bone is maintained as osteoclasts remove bone on the inside and osteoblasts add bone to the outside.

Bone remodeling involves a group of osteoclasts and osteoblasts that travel through or across the surface of bone. These cells remove old bone matrix and replace it with new bone matrix. In compact bone, the osteoclasts break down bone matrix. Osteoblasts move in and lay down a layer of bone. Additional lamellae are produced until an osteon is formed. In spongy bone, the bone matrix is removed from the surface of a trabecula, forming a cavity, which is filled in with new bone matrix.

6.7 BONE REPAIR

Learning Outcome *After reading this section, you should be able to*

A. Outline and explain the steps in bone repair.

Bone is a living tissue that can undergo repair if it is damaged. Figure 6.8 shows the four major steps in bone repair.

PROCESS Figure

PROCESS Figure 6.8 **Bone Repair**

(*a*) On the top is a radiograph of the broken humerus of author A. Russo's granddaughter. On the bottom is the same humerus a few weeks later, with a callus now formed around the break. (*b*) The steps in bone repair.

(a) ©Andrew F. Russo

Suppose an astronaut who currently lives in the international space station fractured a bone. The doctor in the space station told her to expect bone repair to take 8 weeks. If the astronaut experienced the same bone fracture while living on Earth, do you think the expected bone repair time would be shorter or longer than 8 weeks?

CLINICAL IMPACT

Classification of Bone Fractures

Bone fractures are classified in several ways. The most commonly used classification involves the severity of the injury to the soft tissues surrounding the bone. An **open fracture** (formerly called a *compound fracture*) occurs when an open wound extends to the site of the fracture or when a fragment of bone protrudes through the skin. If the skin is not perforated, the fracture is called a **closed fracture** (formerly called a *simple fracture*). If the soft tissues around a closed fracture are damaged, it is called a **complicated fracture.**

Figure 6.9 illustrates several other types of bone fractures. An **incomplete fracture** does not extend completely across the bone, whereas in a **complete fracture** the bone is broken into at least two fragments. An incomplete fracture on the convex side of the curve of the bone is a **greenstick fracture. Hairline fractures** are incomplete fractures in which the two sections of bone do not separate; hairline fractures are common in the skull.

Figure 6.9 Types of Bone Fractures

©Science of the White Blood Cell.

A **comminuted** (KOM-i-noo-ted) **fracture** is a complete fracture in which the bone breaks into more than two pieces—usually two major fragments and a smaller fragment. In an **impacted fracture,** one fragment is driven into the spongy portion of the other fragment.

Fractures are also classified according to the direction of the fracture within the bone. **Linear fractures** run parallel to the length of the bone, and **transverse fractures** are at right angles to the length of the bone. **Spiral fractures** take a helical course around the bone, and **oblique fractures** run obliquely in relation to the length of the bone. **Dentate fractures** have rough, toothed, broken ends, and **stellate fractures** have breakage lines radiating from a central point.

❶ *Hematoma formation*. A **hematoma** (hee-mah-TOH-mah) is a localized mass of blood released from blood vessels but confined within an organ or a space. When a bone is fractured, the blood vessels in the bone and surrounding periosteum are damaged and a hematoma forms. Usually the blood in a hematoma forms a clot, which consists of fibrous proteins that stop the bleeding. Disruption of blood vessels in the central canals results in inadequate blood delivery to osteocytes, and bone tissue adjacent to the fracture site dies. Tissues around the bone often become inflamed and swollen following the injury.

❷ *Callus formation*. A **callus** (KAL-us) is a mass of bone tissue that forms at a fracture site. Several days after the fracture, blood vessels grow into the clot. As the clot dissolves, (a) macrophages clean up cell debris, (b) osteoclasts break down dead bone tissue, and (c) fibroblasts produce collagen and other extracellular materials to form granulation tissue, the precursor to healed tissue (see chapter 4).

A collar is formed around the opposing ends of the bone fragments. Osteoblasts and chondroblasts from the periosteum produce bone and cartilage. The callus is a bone-cartilage collar that stabilizes the ends of the broken bone. In modern medical practice, applying a cast or surgically implanting metal supports can help stabilize the bone.

❸ *Callus ossification*. Like the cartilage models formed during fetal development, the cartilage in the callus is replaced by spongy bone through endochondral ossification. The result is a stronger external callus.

❹ *Bone remodeling*. Repair is complete only when the new bone of the callus and the dead bone adjacent to the fracture site have been replaced by compact bone. In this compact bone, osteons from both sides of the break extend across the fracture line to "peg" the bone fragments together. This remodeling process takes time—as much as a year or more. Eventually, repair may be so complete that no evidence of the break remains; however, the repaired zone usually remains slightly thicker than the adjacent bone. If the fracture has occurred in the diaphysis of a long bone, remodeling also restores the medullary cavity.

6.8 CALCIUM HOMEOSTASIS

Learning Outcomes *After reading this section, you should be able to*

A. Explain the role of bone in calcium homeostasis.

B. Describe how parathyroid hormone and calcitonin influence bone health and calcium homeostasis.

Calcium is a critical physiological regulator of many processes required to achieve and maintain homeostasis. The processes include: (1) stimulation of skeletal muscle contraction, (2) stimulation and regulation of cardiac muscle contraction, and (3) exocytosis of cellular molecules, including those important for neural signaling (see chapters 7, 8, and 12). Because bone is the major storage site for Ca^{2+} in the body, the cells governing bone reabsorption and bone deposition are targets for Ca^{2+}-regulation hormones. In addition to regulating blood Ca^{2+} levels, interactions between osteoclasts, osteoblasts, and Ca^{2+}- regulating hormones also contribute to bone growth, remodeling, and repair (figure 6.10). When osteoblast and osteoclast activities are balanced, the movements of Ca^{2+} into and out of bone are equal. However, if blood Ca^{2+} levels are abnormally depleted for too long, excess Ca^{2+} is released from bone, causing it to become overly demineralized and weak. When blood Ca^{2+} levels are low, osteoclast activity increases and bone reabsorption occurs. Osteoclasts release more Ca^{2+} from bone into the blood than osteoblasts remove from the blood to make new bone. Consequently, a net movement of Ca^{2+} occurs from bone into blood, and blood Ca^{2+} levels increase. Conversely, if blood Ca^{2+} levels are high, osteoclast activity decreases. Osteoclasts release less Ca^{2+} from bone into the blood than osteoblasts remove from the blood for bone deposition. As a result, net movement of Ca^{2+} occurs from the blood to bone, and blood Ca^{2+} levels decrease. Calcium homeostasis is regulated by three hormones (chemical messengers delivered via the blood): (1) parathyroid hormone (PTH); (2) calcitriol, a biologically active form of vitamin D_3; and (3) calcitonin.

Homeostasis Figure 6.10 **Regulation of Blood Ca^{2+} Levels**

(1) Blood Ca^{2+} levels are in the normal range. (2) Blood Ca^{2+} levels increase outside their normal range, which causes homeostasis to be disturbed. (3) The control centers respond to the change in blood levels. (4) The control center releases calcitonin, which inhibits osteoclasts. (5) Reduced osteoclast activity causes blood Ca^{2+} levels to decrease. (6) Ca^{2+} levels return to their normal range and homeostasis is restored. Observe the responses to a decrease in blood Ca^{2+} levels outside the normal range by following the *red arrows in the bottom panel.*

Parathyroid Hormone

Parathyroid hormone is secreted by cells in the parathyroid gland and is essential for the maintenance of blood Ca^{2+} levels within the homeostatic limits. PTH production and secretion are controlled by Ca^{2+}-sensing receptors in the parathyroid gland. The

key signal for PTH secretion is a reduction in blood Ca^{2+} levels. PTH works through two general mechanisms: (1) direct effects on bone cells and in the kidney and (2) indirect effects on the small intestine.

Direct Effects of PTH

Bone Cells

PTH increases blood Ca^{2+} levels by exerting direct regulatory control of osteoblasts and osteocytes to increase formation and activation of osteoclasts, the principal bone-reabsorbing cells. Binding of PTH to its receptor in osteoblast and osteocyte cell membranes stimulates an increased number of active osteoclasts. Further, PTH increases blood Ca^{2+} levels by preventing inhibition of osteoclast formation. It is interesting to note that PTH has been found to also promote bone deposition. Although contradictory to PTH's known bone reabsorption function, giving patients PTH intermittently rather than continuously helps prevent osteoporosis (bone demineralization) from progressing. However, the exact mechanism for PTH stimulation of bone formation is as yet unclear.

Kidney Tubules

PTH stimulates the reabsorption of Ca^{2+} from urine in the kidney tubules, which reduces the amount of Ca^{2+} excreted in the urine.

Indirect Effects of PTH in the Small Intestine

PTH regulates blood Ca^{2+} levels by indirectly increasing Ca^{2+} uptake from the small intestine (see figure 6.10). Increased PTH promotes the activation of calcitriol in the kidneys. Calcitriol increases absorption of Ca^{2+} in the small intestine.

Calcitriol

Calcitriol increases blood Ca^{2+} levels. It is a steroid hormone derived from vitamin D_3. Recall from chapter 5 that vitamin D3 production is initiated in the skin and continued in the liver and then in the kidney, where calcitriol activation occurs. PTH stimulates calcitriol activation in the kidney, which contributes to PTH-induced increases in blood Ca^{2+} levels. Calcitriol and PTH work together to increase osteoclast activity for bone reabsorption. In addition, calcitriol assists PTH in the kidney tubules by preventing Ca^{2+} removal through urine. These actions of calcitriol increase blood Ca^{2+} levels.

Calcitonin

Calcitonin (KAL-si-TOH-nin) is secreted from C cells in the thyroid gland when blood Ca^{2+} levels are too high. Calcitonin rapidly lowers blood Ca^{2+} levels by inhibiting osteoclast activity (see figure 6.10). However, the exact role of calcitonin, especially in adult bone remodeling, is still under investigation. PTH and calcitonin are described more fully in chapters 10 and 18.

MICROBES IN YOUR BODY

Disruption of Bone Homeostasis by Bacteria

Osteomyelitis is a bacterial infection in bone. Usually, the aggressive pathogen *Staphylococcus aureus* is the causative organism. This bacterium is more commonly found on our skin but can move into bone in three major ways: (1) The bacterium spreads to the bone through the bloodstream from another infected location in the body, such as an abscessed tooth; (2) it penetrates the bone through an open wound on the skin, which may occur in severe cases of diabetes; and (3) it is introduced into a joint or bone during surgery—for example, while putting a pin in a broken bone. Once bacteria are in the bone, their presence induces a severe inflammatory response, which is then followed by progressive bone loss.

During infection, osteoblasts are co-opted to overactivate osteoclasts, the bone-destroying cells.

Staphylococcus aureus cell walls contain a certain cell marker that alters signaling dynamics in such a way that the production of osteoclasts increases but the production of osteoblasts decreases. Bacterial infection prevents normal functioning of the bone-forming osteoblasts.

The final result is that although the host's immune response is designed to remove the infection, it results in massive damage of the host's own tissues.

The most common treatment for osteomyelitis is a 4- to 8-week course of antibiotics. The doctor may prescribe intravenous dosing with the antibiotics; thus, patients are often fitted with a peripherally inserted central catheter (PICC) line. If the infection persists, it may be necessary to perform surgery in which the infected tissue is removed, in a process called debridement. In cases of severe tissue damage, a bone graft is necessary. Fortunately, the incidence of osteomyelitis is low, 2 in 10,000 people, and the majority of osteomyelitis cases are successfully resolved.

Understand ***Apply It 3***

In addition to targeting the bacteria for death, what is one theoretical medical approach that could help reduce the amount of bone loss during osteomyelitis?

6.9 SKELETAL ANATOMY OVERVIEW

Learning Outcomes ***After reading this section, you should be able to***

A. List and define the major features of a typical bone.
B. List the two anatomical portions of the skeleton.
C. List the bone shapes.

The average adult has 206 bones (table 6.1; figure 6.11). However, the actual number of bones varies among people and decreases with age as bones become fused. Bones are segregated into the **axial skeleton** and the **appendicular skeleton** (see figure 6.11). The axial skeleton consists of the bones of the skull, the auditory ossicles, the

hyoid bone, the vertebral column, and the thoracic cage (rib cage). The appendicular skeleton consists of the bones of the **upper limbs,** the **lower limbs,** and the two **girdles.** The term *girdle,* which means "belt" or "zone," refers to the two zones where the limbs are attached to the body. These two zones are the **pectoral girdle** and the **pelvic girdle.**

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Table 6.1 Number of Named Bones Listed by Category

Bones		**Number**
Axial Skeleton		
Skull (Cranium)		
Cranial bones		
Paired (left and right)	Parietal	2
	Temporal	2
Unpaired (single)	Frontal	1
	Sphenoid	1
	Occipital	1
	Ethmoid	1
Facial bones		
Paired	Maxilla	2
	Zygomatic	2
	Palatine	2
	Lacrimal	2
	Nasal	2
	Inferior nasal concha	2
Unpaired	Mandible	1
	Vomer	1
	Total skull bones	22
Bones Associated with the Skull		
Auditory ossicles		
Malleus		2
Incus		2
Stapes		2
Hyoid		1
	Total associated bones	7
Vertebral Column		
Cervical vertebrae		7
Thoracic vertebrae		12
Lumbar vertebrae		5

Bones		**Number**
Sacrum		1
Coccyx		1
	Total vertebral column bones	26
Thoracic Cage		
Ribs		24
Sternum		1
	Total thoracic cage bones	25
	Total axial skeleton bones	80
Appendicular Skeleton		
Pectoral Girdle		
Scapula		2
Clavicle		2
Upper Limb		
Humerus		2
Ulna		2
Radius		2
Carpal bones		16
Metacarpal bones		10
Phalanges		28
	Total girdle and upper limb bones	64
Pelvic Girdle		
Hip bone		2
Lower Limb		
Femur		2
Tibia		2
Fibula		2
Patella		2
Tarsal bones		14
Metatarsal bones		10
Phalanges		28
	Total girdle and lower limb bones	62
	Total appendicular skeleton bones	126
	Total axial skeleton bones	80
	Total appendicular skeleton bones	126
	Total bones	206

Figure 6.11 APR **Complete Skeleton**

Bones of the axial skeleton are listed in the columns on each side of the figure; bones of the appendicular skeleton are listed in the center of the two skeleton views. (The skeleton is not shown in the anatomical position.)

Bone Shapes

There are four categories of bone, based on their shape: (1) long, (2) short, (3) flat, and (4) irregular. **Long bones** are longer than they are wide. This shape enhances their function in movement of appendages. Most of the bones of the upper and lower limbs are long bones. **Short bones** are approximately as wide as they are long; examples are the bones of the wrist and ankle. Short bones help transfer force between long bones. **Flat bones** have a relatively thin, flattened shape. Flat bones are well-suited to providing a strong barrier around soft organs such as the brain and heart. Examples of flat bones are certain skull bones, the ribs, the scapulae (shoulder blades), and the sternum. **Irregular bones** include the vertebrae and

facial bones, which have shapes that do not fit readily into the other three categories. These bones tend to have specialized functions, such as providing protection while allowing bending and flexing of certain body regions such as the spine.

Skeletal Terminology

Anatomists use several common terms to describe the features of bones (table 6.2). For example, a hole in a bone is called a **foramen** (foh-RAY-men; pl. foramina, foh-RAH-min-ah; *foro,* to pierce). A foramen usually exists in a bone because some structure, such as a nerve or blood vessel, passes through the bone at that point. If the hole is elongated into a tunnel-like passage through the bone, it is called a **canal** or a **meatus** (mee-AY-tus; a passage). A depression in a bone is called a **fossa** (FOSS-ah). A rounded projection on a bone is called a **tubercle** (TOO-ber-kul; a knob) or a **tuberosity** (TOO-ber-OS-i-tee), and a sharp projection from a bone is called a **process.** Most tubercles and processes are sites of muscle attachment on the bone. Increased muscle pull, as occurs when a person lifts weights to build up muscle mass, can increase the size of some tubercles. The smooth, rounded end of a bone, where it forms a joint with another bone, is called a **condyle** (KON-dile; knuckle).

Table 6.2 Anatomical Terms for Features of Bones

Term	Description
Major Features	
Body, shaft	Main portion
Head	Enlarged (often rounded) end
Neck	Constricted area between head and body
Condyle	Smooth, rounded articular surface
Facet	Small, flattened articular surface
Crest	Prominent ridge
Process	Prominent projection
Tubercle, or tuberosity	Knob or enlargement
Trochanter	Large tuberosity found only on proximal femur
Epicondyle	Enlargement near or above a condyle
Openings or Depressions	
Foramen	Hole
Canal, meatus	Tunnel
Fissure	Cleft
Sinus	Cavity
Fossa	Depression

The bones of the skeleton are divided into axial and appendicular portions (figure 6.11).

6.10 AXIAL SKELETON

Learning Outcomes *After reading this section, you should be able to*

A. List the parts of the axial skeleton.
B. Describe the general functions of the axial skeleton.
C. List the major sutures of the skull and the bones they connect.
D. Name the skull bones.
E. Describe the features of the skull bones.
F. Name the bones that compose the orbit of the eye.
G. List the bones and cartilage that form the nasal septum.
H. Describe the locations and functions of the paranasal sinuses.
I. List the bones of the cranium and face.
J. Explain the unique structure of the hyoid bone.
K. Describe the shape of the vertebral column.
L. List the divisions of the vertebral column.
M. State the functions of the vertebral column.
N. Discuss the common features of the vertebrae.
O. Contrast the structure of vertebrae from each region.
P. List the bones and cartilage of the thoracic cage, including the three types of ribs.

The axial skeleton forms the central axis of the body. It protects the brain, the spinal cord, and the vital organs housed within the thorax.

Skull

The skull consists of 8 cranial bones and 14 facial bones, a total of 22 bones (table 6.1 and figures 6.12–6.17). The cranial bones, or **cranium** (KRAY-nee-um), house and protect the brain. Both the exterior and the interior of the skull have visible ridges and lines. Most of these are locations where head and neck muscles attach to the cranium. The cranial bones are connected by immovable joints called **sutures** (see section 6.12). There are four principal sutures: (1) **coronal,** (2) **sagittal,** (3) **lambdoid,** and (4) **squamous.** The specific sutures will be discussed along with the bones they connect. All other skull bones are held together by sutures as well and are named according to the bones they connect. The top of the skull, called the **calvaria** (kal-VAY-ree-ah), is often removed to view the interior of the skull. The facial bones form the basis of the face; contain cavities for the eyes, nose, and mouth; and are the attachment sites for our facial expression muscles. We discuss the fetal skull in section 6.12.

Figure 6.12 **Superior View of the Skull**

Only four bones are visible from a superior view: the frontal bone, the two parietal bones, and a small portion of the occipital bone. (The names of the bones are in bold.)

Cranial Bones

The 8 bones of the cranium include: (1) the frontal bone, (2 and 3) the 2 parietal bones, (4 and 5) the 2 temporal bones, (6) the occipital bone, (7) the sphenoid bone, and (8) the ethmoid bone.

Frontal Bone

The **frontal bone** is connected to the two parietal bones by the **coronal suture** (figures 6.12, 6.13, and 6.14). The frontal bone is most well-known at the "forehead." It forms the roof of both the orbit of the eye and the nasal cavity. The superior border of each of the orbits contains a **supraorbital foramen,** or **notch,** which allows passage of a blood vessel and nerve for the eyelid and eye. Between the two orbits is the **glabella** (smooth), a smooth region of bone. The frontal bone also contains the **frontal sinus,** one of the **paranasal sinuses** (figure 6.15). Internally, the frontal bone forms the **anterior cranial fossa,** which supports lobes of the brain.

Figure 6.13 APR **Right Lateral View of the Skull**

The parietal bone and the squamous part of the temporal bone form a major portion of the side of the head. (The names of the bones are in bold.)

Figure 6.14 **Anterior View of the Skull and Face**

(*a*) The major structures seen from the anterior view are the frontal bone, the zygomatic bones, the maxilla, and the mandible. (The names of the bones are in bold.) (*b*) View of bony landmarks on the anterior of the face.

(b) ©Eric Wise

Figure 6.15 **Paranasal Sinuses**

(a) Anterior view. *(b)* Lateral view. *(c)* X-ray of the sinuses, lateral view. *(d)* X-ray of the sinuses, anterior view.

(c) Hemera Technologies/Getty Images; (d) Hemera Technologies/Getty Images

Parietal Bones

The paired parietal bones form nearly half of the superior portion of the skull (see figure 6.12). The two parietal bones are joined by the **sagittal suture** and are connected to the occipital bone by the **lambdoid suture.** Along with the temporal bones, the parietal bones make up the majority of the lateral portion of the skull.

Temporal Bones

The **temporal bones** are connected to the skull by the **squamous sutures** (see figure 6.13). The term *temporal* means "related to time"; the temporal bone's name is derived from the observation that the hair on the temples turns gray as a person ages. The temporal bone is subdivided into three main regions: (1) the squamous part, (2) the tympanic part, and (3) the petrous part.

1. The **squamous part** of each temporal bone meets the parietal bone. The **zygomatic** (zie-goh-MAT-ik) **process** extends from the squamous part anteriorly toward the zygomatic bone of the face. It joins with the zygomatic bone to form the **zygomatic arch,** a bridge across the side of the skull (see figure 6.13). Note that bone processes are named for the bones to which they extend. The zygomatic process has an oval-shaped fossa on the inferior side, called the **mandibular fossa.** The mandibular fossa is the attachment site of the mandible (lower jaw).
2. The **tympanic part** of the temporal bone has the prominent **external auditory canal** (*external acoustic meatus*), which transmits sound waves toward the eardrum, or tympanic membrane. The external ear surrounds the external acoustic meatus.

3. The **petrous part** of the temporal bone extends inward toward the center of the skull. The petrous part is a thick, bony ridge (petrous; rocky), is hollow, and houses the middle and inner ears. The **internal auditory canal** (figure 6.16) is located on the posterior surface of the petrous part and is the opening for a nerve controlling hearing and balance. Externally, the **mastoid** (MASS-toyd) **process** (see figures 6.13, 6.17) is a large, bony inferior projection that can be seen and felt just posterior to the external ear. This process is not solid bone, but is filled with cavities called **mastoid air cells,** which are connected to the middle ear and can sometimes become infected, causing **mastoiditis.** Neck muscles that rotate the head attach to the mastoid process.

Figure 6.16 APR **Floor of the Cranial Cavity**

(*a*) Drawing of the floor of the cranial cavity. The calvaria of the skull has been removed, and the floor is viewed from above. (*b*) Photo of the same view.

(The names of the bones are in bold.) (b) Christine Eckel/McGraw-Hill Education

Figure 6.17 APR **Inferior View of the Skull**

(*a*) Drawing of an inferior view of the skull with the mandible removed. The base of the skull is complex, with a number of foramina and specialized surfaces. (*b*) Photo of the same view in.

(The names of the bones are in bold.) (b) Christine Eckel/McGraw-Hill Education

The **styloid** (STY-loyd; stylus, or pen-shaped) **process** (see figures 6.13 and 6.17) projects from the lower portion of the petrous part of the temporal bone. The styloid process serves as an attachment site for three muscles necessary for movement of the tongue, hyoid bone, and pharynx. The **stylomastoid foramen** is located between the styloid process and mastoid process and allows for passage of a nerve controlling facial muscles. There are three additional important foramina on the inferior side of the petrous part (see figures 6.16 and 6.17). The **jugular** (JUG-you-lar) **foramina** allow the jugular veins to carry the majority of the blood away from the brain. The **carotid** (kah-ROT-id) **canals** are the major entry point for blood delivery to the brain. The **foramen lacerum** (lah-SER-um; torn) is an easily noticeable opening in a dried skull at the border of the petrous part and the sphenoid bone. However, this foramen is only an artifact of the dried skull; in life, this opening is closed off by cartilage.

Occipital Bone

The **occipital bone** makes up the majority of the skull's posterior wall and base (see figures 6.16, and 6.17). Its most prominent feature is the **foramen magnum** (large hole), the opening where the brainstem connects to the spinal cord (see figures 6.16 and 6.17). This region also forms the **posterior cranial fossae** that support the cerebellum of the brain. Externally, two rounded projections on either side of the foramen magnum are the **occipital condyles** (see figure 6.17). The occipital condyles are the points of articulation between the skull and the first

cervical vertebra. This articulation partly allows for nodding "yes." The **nuchal** (NOO-kal; nape of neck) **lines** are points of attachment for several neck muscles that move the head.

Sphenoid Bone

Although appearing to be two bones, one on each side of the skull anterior to the temporal bone, the **sphenoid** (SFEE-noyd) **bone** is actually a single bone that extends completely across the skull (see figure 6.13). When viewed as a whole, the sphenoid bone somewhat resembles a butterfly.

The center of the sphenoid bone forms a central prominence within the floor of the cranial cavity. The shape of this prominence resembles a saddle, called the **sella turcica** (SEL-ah TUR-sih-kah; Turkish saddle) (see figure 6.16). The sella turcica surrounds and protects the pituitary gland. Within the body of the sphenoid bone are the **sphenoidal sinuses** (see figure 6.15). An **optic canal** is located on each side of the sphenoid bone just anterior to the sella turcica. The optic canal is the passageway for the optic nerve to enter the brain from the eyes. Three additional paired foramina are located on either side of the sella turcica: (1) the **foramen rotundum,** (2) the **foramen ovale (**oh-VAL-ee), and (3) the **foramen spinosum** (see figures 6.16 and 6.17). These foramina are passageways for blood vessels and nerves that service the brain as well as the meninges, protective membranes that surround the brain. The lateral portions of the sphenoid bone (1) form the floor of the **middle cranial fossa,** (2) are a part of the lateral skull wall, and (3) form the posterior wall of the orbits. The sphenoid bone also forms a ridge on each side of the optic canals. This ridge separates the anterior cranial fossa from the middle cranial fossa. Additionally, this ridge is the superior border of the **superior orbital fissure,** where cranial nerves controlling eye movement enter the orbit (see figure 6.14). The pterygoid processes, which extend inferiorly, are attachment sites for muscles of mastication (see figure 6.17).

Ethmoid Bone

The **ethmoid** (ETH-moid; *ethmos,* sieve) **bone** is appropriately named because it is a very porous, fragile bone. It is centrally located in the skull, forming the **nasal septum** (wall), a large portion of the nasal cavity, as well as the medial wall of the orbits. The sinuses within the ethmoid bone form the **ethmoidal sinuses** (see figure 6.15). The **crista galli** (KRIS-tah GAL-ee; rooster's comb) is a prominent ridge of the ethmoid bone. The crista galli is an attachment site for the meninges of the brain. Located on each side of the crista galli are the **cribriform** (KRIB-ri-form; sievelike) **plates,** each of which houses one of the two olfactory bulbs that transmit signals for the sense of smell from the nasal cavity to the brain. The cribriform plates contain numerous foramina, called **olfactory foramina,** which allow olfactory nerves to enter the nasal cavity (see figure 6.14 and chapter 8). Extending inferiorly from the ethmoid bone is a central, thin bony plate called the

perpendicular plate (see figure 6.14). The perpendicular plate forms the superior portion of the nasal **septum,** which divides the nasal cavity into right and left halves. Protruding medially from the ethmoid bone are two scroll-shaped bones called the **conchae** (KON-kee) (see figure 6.14). The **inferior nasal concha** (KON-kah) is a separate bone, which will be discussed later. Together, the three nasal conchae increase the surface area in the nasal cavity, thereby facilitating moistening of and removal of particles from air in the nasal cavity, and warming of the air inhaled through the nose (see chapter 15).

Specialized Regions in the Skull

Paranasal Sinuses

Considered together, the sinuses found in the frontal bone, the ethmoid bone, the sphenoid bone, and the maxilla are called the paranasal sinuses (see figure 6.15). The paranasal sinuses are openings within particular bones that open into the nasal cavity. The sinuses have two major functions: (1) they decrease the weight of the skull and (2) they act as a resonating chamber when speaking. Compare the sound of your voice during a head cold to its sound normally.

Orbits

The orbits (see figure 6.14) are cone-shaped fossae. They are called the orbits because they allow the eyes to rotate within the fossae. Portions of multiple bones converge to form the orbits. The orbits protect the eyes and are the locations where the muscles controlling eye movements attach. The orbits have several openings through which structures communicate between the orbit and other cavities. The nasolacrimal duct passes from the orbit into the nasal cavity through the **nasolacrimal canal,** carrying tears from the eyes to the nasal cavity. The optic nerve for vision passes from the eye through the optic canal and enters the cranial cavity. Superior and inferior orbital fissures in the posterior of the orbits provide openings through which nerves and blood vessels communicate with structures in the orbit or pass to the face.

Understand ***Apply It 4***

Why does your nose run when you cry?

Nasal Cavity

The nasal cavity has a rounded opening anteriorly and is separated into right and left halves by the nasal septum. The posterior part of the nasal septum consists primarily of the perpendicular plate of the ethmoid bone, as discussed earlier, and the vomer bone, to be discussed with the facial bones. Hyaline cartilage forms the anterior part of the nasal septum. The entrances to the nasal cavity in a dried skull are much larger than the openings in a living person. This is because the external nose is formed mostly of hyaline cartilage and will be absent from a dried skull. The

only visible portions of the external nose in a dried skull are (1) the two nasal bones and (2) the maxilla (see figure 6.14).

Facial Bones

The 14 facial bones of the skull include (1 and 2) the pair of zygomatic bones, (3 and 4) the pair of maxilla bones, (5 and 6) the pair of palatine bones, (7 and 8) the pair of lacrimal bones, (9 and 10) the pair of nasal bones, (11) the mandible, (12) the vomer bone, and (13 and 14) the pair of inferior nasal conchae (see table 6.1). These bones, in addition to two cranial bones (the frontal and ethmoid bones), form the structure of the face in the anterior of the skull. The facial bones protect the major sensory organs located in the face: the eyes, nose, and tongue. These bones also provide attachment points for muscles controlling mastication, facial expressions associated with our emotions, and eye movements. It is the bones of the face and their soft tissues that determine the uniqueness of each individual's facial appearance.

Zygomatic Bones

The **zygomatic** (zie-goh-MAT-ik) **bones,** commonly known as the cheekbones, are anterior to the sphenoid bone (see figure 6.13). There they form part of the border of the orbits. As previously discussed, the temporal process of the zygomatic bone articulates with the zygomatic process of the temporal bone to form the **zygomatic arch.**

Maxillae

Each **maxilla** (mak-SIL-ah; pl. maxillae, upper jaw) is anterior and inferior to the zygomatic bones, and the two maxillae are fused in the center (see figures 6.14 and 6.17). The maxillae are two of the three jaw bones, and form (1) the upper jaw, (2) the majority of the roof of the mouth, and (3) the center portion of the face. Each of the two maxillary bones has a **palatine process.** These join medially to form the anterior two-thirds of the **hard palate,** or the roof of the mouth. The **incisive foramen** is located just posterior to the front teeth and allows passage of blood vessels and nerves. The posterior one-third is formed by two other facial bones, the palatine bones to be discussed later. The palate separates the nasal cavity from the mouth, enabling humans to chew and breathe at the same time.

Below the orbits, within each maxilla is an **infraorbital foramen** for passage of a facial nerve and artery (see figure 6.14). At the junction of the maxilla with the greater wing of the sphenoid bone is the **inferior orbital fissure** (see figure 6.14). This fissure allows the passage of several nerves and blood vessels to the face.

Palatine Bones

The **palatine bones** have horizontal plates that fuse centrally to form the posterior portion of the hard palate as described earlier with the maxillae.

Lacrimal Bones

The **lacrimal** (LAK-rim-al; tears) **bones** are the smallest of the skull bones and house the depression through which the nasolacrimal duct enters the nasolacrimal canal, joining the orbits and nasal cavity (see figure 6.14 and chapter 9).

Nasal Bones

The **nasal bones,** along with the frontal processes of the maxillae, form the bridge of the nose.

Mandible

The **mandible** (lower jaw) is the only skull bone that is freely movable relative to the other skull bones. It is inferior to the maxillae and attaches posteriorly to the temporal bone via the **mandibular fossae** (see figure 6.13). The mandible joins the temporal bone by way of the attachment of the **mandibular condyle** with the mandibular fossa. The **coronoid** (KOR-oh-noyd) **process** is anterior to the mandibular condyle. The powerful muscle of mastication, the temporalis muscle, attaches to the coronoid process. On each anterior surface of the mandible is the **mental foramen** for passage of nerves and blood vessels to the chin.

Vomer

The **vomer** forms most of the posterior portion of the nasal septum (see figure 6.14).

Inferior Nasal Conchae

The **inferior nasal concha,** as discussed with the ethmoid bone, is one of the three conchae in the nasal cavity that provide increased surface area (see figure 6.14).

Hyoid Bone

The **hyoid bone** (figure 6.18) is important for speech and swallowing. Some tongue muscles as well as neck muscles that elevate the larynx attach to the hyoid. The hyoid bone is unpaired, and is often listed as part of the facial bones. However, it is not part of the adult skull (see table 6.1). The hyoid bone has the unique distinction of being the only bone in the body not directly attached to another bone. It has no direct bony attachment to the skull. Instead, muscles and ligaments attach it to the skull, so the hyoid is embedded in soft tissue in the neck just below the mandible.

Figure 6.18 **Hyoid Bone**

Anterior and lateral views of the hyoid bone. The only bone in the body that does not attach to another bone.

Vertebral Column

The **vertebral column** performs five major functions: (1) It supports the weight of the head and trunk, (2) it protects the spinal cord, (3) it allows spinal nerves to exit the spinal cord, (4) it provides a site for muscle attachment, and (5) it permits movement of the head and trunk. The vertebral column usually consists of 26 bones, called **vertebrae,** which can be divided into five regions: 7 **cervical vertebrae** (VER-teh-bray), 12 **thoracic vertebrae,** 5 **lumbar vertebrae,** 1 **sacral bone,** and 1 **coccygeal** (kok-SIJ-ee-al) **bone** (figure 6.19). For convenience, each of the five regions is identified by a letter, and the vertebrae within each region are numbered: C1–C7, T1–T12, L1–L5, S, and CO. You can remember the number of vertebrae in the non-fused regions of the vertebral column by remembering mealtimes: 7, 12, and 5. The developing embryo has about 33 or 34 vertebrae, but by adulthood the 5 sacral vertebrae have fused to form 1 bone, and the 4 or 5 coccygeal bones usually have fused to form 1 bone.

Figure 6.19 APR **Vertebral Column**

The complete vertebral column is viewed from the left side.

The adult vertebral column has four major curvatures (figure 6.19). The cervical region curves anteriorly, the thoracic region curves posteriorly, the lumbar region curves anteriorly, and the sacral and coccygeal regions together curve posteriorly.

The curves form during embryonic development. Because the embryo and fetus are C-shaped within the uterus, the vertebral column is naturally curved from the beginning. After birth, when the infant raises its head, a secondary curve, which curves anteriorly, develops in the cervical region. Later, when the infant learns to sit and then walk, the lumbar portion of the column also becomes curved anteriorly. These spinal curvatures help accommodate our upright posture by aligning our body weight with our pelvis and lower limbs.

General Features of the Vertebrae

Each vertebra consists of (1) a body, (2) a vertebral arch, and (3) various processes (figure 6.20). Two specific portions of the vertebrae help support the body's weight and protect the spinal cord. The **vertebral body,** the solid bony disk of each vertebra, supports the body's weight.

Figure 6.20 Vertebra
Superior view of a generalized vertebra.

The **vertebral arch,** along with the body, protects the spinal cord. The vertebral arch projects posteriorly from the body. Together, the vertebral arch and the body form a complete bony circle enclosing the **vertebral foramen,** which is occupied by the spinal cord in a living person. The vertebral foramina of adjacent vertebrae combine to form the **vertebral canal,** which contains the entire spinal cord and cauda equina (see figure 8.14). The vertebral arch is divided into left and right halves, and each half has two parts: (1) the **pedicle** (PED-ih-kul; foot), which is attached to the body, and (2) the **lamina** (LAM-i-na; thin plate), which forms the posterior portion of the vertebral foramen.

A **transverse process** extends laterally from each side of the arch between the lamina and the pedicle, and a single **spinous process** lies at the junction between the two laminae. The spinous processes can be seen and felt as a series of rounded projections down the midline of the back (figure 6.19). Much vertebral movement is accomplished by the contraction of the skeletal muscles attached to the transverse

and spinous processes (see chapter 7). The **intervertebral foramina** are the locations where two vertebrae meet (see figure 6.19). Each intervertebral foramen is formed by **intervertebral notches** in the pedicles of adjacent vertebrae. These foramina are where spinal nerves exit the spinal cord.

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Movement and additional support of the vertebral column are made possible by the vertebral processes. Each vertebra has two **superior** and two **inferior articular processes,** with the superior processes of one vertebra articulating with the inferior processes of the next superior vertebra. Overlap of these processes increases the rigidity of the vertebral column. The region of overlap and articulation between the superior and inferior articular processes creates a smooth **articular facet** (FAS-et; little face) on each articular process. In a living person, vertebrae are separated by **intervertebral disks.**

Regional Differences in Vertebrae

Each of the five regions of the vertebral column has uniquely shaped vertebrae that contribute to the particular function of each region of the vertebral column. As one region gives way to another region, the characteristics between regional vertebrae become less distinct (figure 6.21).

Figure 6.21 APR **Regional Differences in Vertebrae**

The posterior portion lies at the top of each illustration. (*a*) Superior view of the atlas. (*b*) Superior view of the axis. (*c*) Superior view of a generic cervical vertebra. (*d*) Superior view of a generic thoracic vertebra. (*e*) Superior view of a generic lumbar vertebra.

(a) (1) Christine Eckel/McGraw-Hill Education

Cervical Vertebrae

Cervical vertebrae are located in the vertebral column region with the greatest range of motion. These vertebrae support and move the head (figure 6.19). However, because the cervical vertebrae support only the weight of the head, they have very small bodies, making dislocations and fractures in this area of the vertebral column more common than in other regions. Cervical vertebrae are also unique in that the transverse processes have **transverse foramina** through which the vertebral arteries extend toward the head.

The first two cervical vertebrae include (1) the **atlas** (C1) and (2) the **axis** (C2) (figure 6.21). The atlas and axis are heftier than the other five cervical vertebrae because they directly support the weight of the head and control its movements. The atlas derives its name from the Greek mythology character, Atlas, who held the world (the head) on his shoulders. The atlas does not have a body or a spinous process. The connection between the occipital condyles and the superior articular facets forms a joint that allows you to nod your head "yes" (see section 6.12).

The axis is so named because the joint between the atlas and the axis allows for a significant amount of head rotation. Shaking your head "no" occurs when the atlas rotates on the axis. This rotation occurs around the highly modified superior process of the axis, called the **dens.**

Thoracic Vertebrae

In contrast to the large degree of motion of the cervical region, the thoracic region is the least moveable of the five regions due to the articulation of the thoracic vertebrae with the ribs. The **thoracic vertebrae** support the thoracic cage, which houses and protects the heart and lungs (figure 6.21; see figures 6.19 and 6.23). These vertebrae have the longest spinous processes, which project inferiorly. In addition, their transverse processes are longer than others, and the first 10 possess **articular facets** for the ribs. The bodies have articular facets for the heads of the ribs.

Lumbar Vertebrae

The **lumbar vertebrae** support the majority of the body's weight (6.21; see figure 6.19). Consequently, they have massive bodies and heavy, rectangular transverse and spinous processes. The thickness of the bodies makes fractures of the lumbar vertebrae less common, but ruptured intervertebral disks are more common in this area than in other regions of the vertebral column. The fifth lumbar vertebra or first

coccygeal vertebra may become fused into the sacrum. Conversely, the first sacral vertebra may fail to fuse with the rest of the sacrum, resulting in six lumbar vertebrae. The information in this section may be helpful when answering this chapter's Learn to Apply It question.

Sacrum

The **sacrum** is located between the two hip bones (figure 6.22; see figures 6.19 and 6.30). The sacrum is formed from five separate sacral vertebrae that begin to fuse during adolescence, resulting in a solid bony plate by the mid-20s. The sacrum is part of the pelvic girdle, which provides stable support for our lower limbs. The pelvic girdle will be described more fully with the appendicular skeleton.

Figure 6.22 APR **Sacrum**

(*a*) Anterior view of the sacrum. (*b*) Posterior view of the sacrum. (*c*) Photo of the posterior view of the sacrum.

(c) Christine Eckel/McGraw-Hill Education

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The former spinous processes, now partially fused, form a ridge called the **median sacral crest.** At the inferior surface of the sacrum, there is an opening, called the **sacral hiatus** (high-AYE-tus; gap), which is the termination of the vertebral canal. The sacral hiatus is a common anesthesia injection site.

The first sacral vertebra bulges anteriorly into the pelvic cavity. This bulge is called the sacral promontory (see figure 6.19). It is used as a clinical landmark for separation of the abdominal cavity and the pelvic cavity.

Coccyx

The **coccyx** (KOK-siks) is commonly referred to as the tailbone (figure 6.22; see figure 6.19). It is the terminal portion of the vertebral column. It can be formed from three to five semi-fused vertebrae. In males the coccyx may project anteriorly, but in females it often projects more inferiorly. These vertebrae are much smaller than the

other vertebrae and have neither vertebral foramina nor well-developed processes. The coccyx is easily broken when a person falls by sitting down hard on a solid surface.

Thoracic Cage

The **thoracic cage,** commonly called the rib cage, protects the heart and lungs within the thorax. It forms a semirigid chamber, which can increase and decrease in volume during respiration. It consists of (1) the thoracic vertebrae, (2) the ribs with their associated costal (rib) cartilages, and (3) the sternum (figure 6.23).

Figure 6.23 APR **Thoracic Cage**
Entire thoracic cage as seen from an anterior view.

Ribs and Costal Cartilages

There are 12 pairs of **ribs.** Ribs are classified as either true ribs or false ribs. Ribs 1–7 are called **true ribs.** True ribs attach directly through **costal cartilage** to the sternum. Ribs 8–12 are called **false ribs** because they do not attach directly to the sternum. The false ribs consist of two groups. Ribs 8–10 are joined by a common cartilage to the costal cartilage of rib 7, which in turn is attached to the sternum. Two of the false ribs, ribs 11 and 12, are also called **floating ribs** because they do not attach to the sternum. The costal cartilages are flexible and permit the thoracic cage to expand during respiration.

Sternum

The **sternum,** or breastbone, has been described as sword-shaped and has three parts (figure 6.23): (1) The **manubrium** (mah-NOO-bree-um; handle) is the "sword handle"; (2) the **body,** or gladiolus (sword), is the "blade"; and (3) the **xiphoid** (ZI-

foyd; sword) **process** is the "sword tip." The superior margin of the manubrium has a **jugular** (suprasternal) **notch** in the midline, which can be easily felt at the anterior base of the neck. The first rib and the clavicle articulate with the manubrium. The point at which the manubrium joins the body of the sternum can be felt as a prominence on the anterior thorax called the **sternal angle** (see figure 6.23). The cartilage of the second rib attaches to the sternum at the sternal angle, the third through seventh ribs attach to the body of the sternum, and no ribs attach to the xiphoid process.

6.11 APPENDICULAR SKELETON

Learning Outcomes *After reading this section, you should be able to*

A. Identify the bones that make up the pectoral girdle.
B. Relate the pectoral girdle bones' structure and arrangement to the function of the pectoral girdle.
C. Name the major bones of the upper limb.
D. Describe the major bones of the upper limb.
E. Name the bones of the pelvic girdle.
F. Describe the bones of the pelvic girdle.
G. Explain why the pelvic girdle is more stable than the pectoral girdle.
H. Name the bones that make up the hip bone.
I. Distinguish between the male and female pelvis.
J. Identify the bones of the lower limb.
K. Describe the bones of the lower limb.

The appendicular skeleton allows movement of our appendages and supports our weight in an upright position.

Pectoral Girdle and Upper Limb

Picture a baseball pitcher winding up to throw a fastball and you have a great demonstration of the mobility of your upper limb (figure 6.24). This mobility is possible because muscles attach the upper limb and its girdle rather loosely to the rest of the body. Thus, the upper limb is capable of a wide range of movements, including throwing, lifting, grasping, pulling, and touching.

Figure 6.24 **Bones of the Pectoral Girdle and Right Upper Limb**
Anterior view of the bones of the pectoral girdle and upper limb.

Pectoral Girdle: Scapula and Clavicle

The **pectoral** (PEK-toh-ral) **girdle** consists of two pairs of bones that attach each of the upper limbs to the body. Each pair is composed of a **scapula** (SKAP-you-lah), commonly known as the shoulder blade (figure 6.25), and a **clavicle** (KLAV-i-kul), commonly known as the collarbone (see figures 6.23, 6.24, and 6.25). The scapula is a flat, triangular bone that can easily be seen and felt in a living person.

Figure 6.25 APR **Right Scapula and Clavicle**

(*a*) Right scapula, anterior view. (*b*) Right scapula, posterior view. (*c*) Right clavicle, superior view. (*d*) Photograph of the right scapula and clavicle from a superior view, showing the relationship between the distal end of the clavicle and the acromion process of the scapula.

(d) Christine Eckel/McGraw-Hill Education

At the tip of the shoulder, there is the large **acromion (**ah-CROH-mee-on; shoulder tip) process of the scapula. The **scapular spine** extends from the acromion process across the posterior surface of the scapula. The smaller coracoid (crow's beak) process provides attachments for some shoulder and arm muscles. A **glenoid** (gLEE-noyd, gLEN-oyd) cavity, located in the superior lateral portion of the bone, articulates with the head of the humerus.

The clavicle (see figures 6.23, 6.24, and 6.26*c*) is a long bone with a slight sigmoid (S-shaped) curve. It is easily seen and felt in the living human. It articulates with the scapula and the sternum. On the lateral end it articulates with the acromion process. On the medial end it articulates with the manubrium of the sternum. These are the only bony connections between the pectoral girdle and the axial skeleton. Because the clavicle holds the upper limb away from the body, it facilitates the limb's mobility.

Figure 6.26 **Right Humerus**

(*a*) Anterior view of the right humerus. (*b*) Posterior view of the right humerus. (*c*) Photo of the anterior view of the right humerus.

(c) Christine Eckel/McGraw-Hill Education

Arm: Humerus

The arm, the part of the upper limb from the shoulder to the elbow, contains only one bone, the **humerus** (figure 6.26). The humeral **head** articulates with the glenoid cavity of the scapula. The **anatomical neck,** immediately distal to the head, is almost nonexistent; thus, a surgical neck has been designated. The **surgical neck** is so named because it is a common fracture site that often requires surgical repair. Removal of the humeral head due to disease or injury occurs down to the level of the surgical neck.

The proximal end of the humerus has two prominent landmarks, both sites of muscle attachment: (1) Laterally, it is the **greater tubercle.** (2) Anteriorly, it is the **lesser tubercle.**

The diaphysis of the humerus has a noticeable lateral landmark. The **deltoid tuberosity** is the site of attachment of the deltoid muscle. The distal end of the humerus has several unique features where it articulates with the two forearm bones at the elbow. Laterally, the humerus articulates with the radius. This location is called the **capitulum** (kah-PIT-you-lum; head-shaped). Medially, the humerus articulates with the ulna. This location is called the **trochlea** (TROK-lee-ah; spool). Forearm muscles attach to the humerus just superior to the capitulum and trochlea. The attachment sites are the **medial epicondyle** and the **lateral epicondyle.**

Posteriorly, on the distal end, is a large fossa called the **olecranon** (oh-LEK-rah-non; elbow) **fossa,** which accommodates a portion of the ulna that is easily felt as the point of the elbow.

Forearm: Ulna and Radius

The forearm has two bones: (1) the **ulna** and (2) the **radius** (figure 6.27). The ulna is medial, the same side as the little finger, and the radius is lateral, the same side as the thumb. Recall from chapter 1 that the body is in anatomical position when the palm of the hand faces anteriorly. The ulna and radius articulate with the humerus at the elbow joint. There are several unique features of these two bones at the site of attachment to the humerus.

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Figure 6.27 APR **Right Ulna and Radius**

(*a*) Anterior view of the right ulna and radius. (*b*) Photo of the same view of the right ulna and radius. (*c*) Proximal ends of the right ulna and radius.

(b) Christine Eckel/McGraw-Hill Education

Ulna

The portion of the ulna that articulates with the humerus is the C-shaped **trochlear notch.** The trochlear notch rotates over the trochlea of the humerus when bending the elbow. The anterior surface of the proximal end of the ulna has a process called the **coronoid process.** The coronoid process inserts into a fossa of the humerus when the elbow is bent. The posterior surface of the proximal end of the ulna has a much larger process called the **olecranon process.** The olecranon process inserts into the olecranon fossa of the humerus when the elbow is straightened.

On the distal end of the ulna, on the medial side, is the **head** of the ulna. The head of the ulna articulates with both the radius and the wrist bones (see figures 6.27 and 6.28). On the distal end of the ulna, on the lateral side, there is a small process called the **styloid** (STY-loyd; stylus) **process.** Ligaments of the wrist attach to the styloid process.

Figure 6.28 APR **Bones of the Right Wrist and Hand**
Posterior view of the bones of the right wrist and hand.

Radius

The portion of the radius that articulates with the humerus is the **head.** The head of the radius rotates over the capitulum of the humerus when bending the elbow. Just inferior to the radial head on the medial side is the **radial tuberosity,** the site of attachment for the biceps brachii muscle of the arm.

The distal end of the radius also has a **styloid process.** The styloid process of the radius is lateral and also serves as an attachment location for wrist ligaments.

Wrist: Carpals

The wrist is a relatively short region between the forearm and the hand; it is composed of eight **carpal** (KAR-pal) **bones** arranged into two rows of four each (figure 6.28). The proximal row of carpal bones, lateral to medial, includes (1) the **scaphoid** (SKAF-oid), which is boat-shaped; (2) the **lunate** (LOO-nayt), which is moon-shaped; (3) the three-cornered **triquetrum** (try-KWEE-trum, try-KWET-rum); and (4) the pea-shaped **pisiform** (PIS-i-form), which is located on the palmar surface of the triquetrum. The distal row of carpal bones, from medial to lateral, includes (1) the **hamate** (HA-meyt), which has a hooked process on its palmar side, called the hook of the hamate; (2) the head-shaped **capitate** (KAP-i-tate); (3) the **trapezoid** (TRAP-e-zoid), which is named for its resemblance to a four-sided geometric form with two parallel sides; and (4) the **trapezium** (tra-PEE-zee-um), which is named after a four-sided geometric form with no two sides parallel. A number of mnemonics have been developed to help students remember the carpal bones. The following one represents them in order from lateral to medial for the proximal row (top) and from medial to lateral (by the thumb) for the distal row: **S**traight **L**ine **T**o **P**inky, **H**ere **C**omes **T**he **T**humb—that is, **S**caphoid, **L**unate, **T**riquetrum, **P**isiform, **H**amate, **C**apitate, **T**rapezoid, and **T**rapezium.

Hand: Metacarpals and Phalanges

Five **metacarpal bones** are attached to the carpal bones and make up the central portion of the hand (figure 6.28). They are numbered one to five, starting with the most lateral metacarpal bone, at the base of the thumb. The metacarpal bones form a curve so that, in the resting position, the palm of the hand is concave. The distal ends of the metacarpal bones help form the knuckles of the hand. The spaces between the metacarpal bones are occupied by soft tissue.

The five **digits** of each hand include one thumb (**pollex**) and four fingers. Each digit consists of small long bones called **phalanges** (fah-LAN-jeez; sing. phalanx). The thumb has two phalanges, called proximal and distal. Each finger has three phalanges, designated proximal, middle, and distal.

Pelvic Girdle and Lower Limb

The lower limbs support the body and are essential for normal standing, walking, and running. The general pattern of the lower limb (figure 6.29) is very similar to that of the upper limb, except that the pelvic girdle is attached much more firmly to the body than the pectoral girdle is and the bones in general are thicker, heavier, and longer than those of the upper limb. These structures reflect the function of the lower limb in supporting and moving the body.

Figure 6.29 **Bones of the Pelvic Girdle and Right Lower Limb**
Anterior view of the bones of the pelvic girdle and right lower limb.

Pelvic Girdle: Hip Bones and Sacrum

Hip Bones

The **pelvic girdle** is formed by the two **hip bones** (*coxal bones*) and the sacrum (see figure 6.29). The hip bones join each other anteriorly and connect with the sacrum posteriorly forming a complete circle of bone. The **pelvis** (PEL-vis; basin) includes the pelvic girdle and the coccyx (figure 6.30).

Figure 6.30 **Pelvis**

Anterosuperior view of the bones of the articulated pelvis.

Each hip bone is a large bony plate formed from the fusion of three separate bones: (1) the **ilium** (IL-ee-um; groin), (2) the **ischium** (IS-kee-um; hip), and (3) the **pubis** (PYOO-bis; genital hair) (figure 6.31). The three individual bones converge near the center of the hip socket, called the **acetabulum** (as-eh-TAB-you-lum; vinegar cup). The lower limbs articulate with the pelvic girdle in the acetabulum.

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Figure 6.31 APR **Right Hip Bone**

(*a*) Right hip bone, lateral view. Each hip bone is formed by fusion of the ilium, ischium, and pubis. The three bones can be seen joining near the center of the acetabulum, separated by lines of cartilage. (*b*) Medial view of the right hip bone. (*c*) Photo of the lateral view of the right hip bone.

(The names of the three bones forming the hip bone are in bold.) (c) Christine Eckel/McGraw-Hill Education

The articular surface of the acetabulum is crescent-shaped and occupies only the superior and lateral aspects of the fossa. The pelvic girdle serves as the place of attachment for the lower limbs, supports the weight of the body, and protects internal organs. Because the pelvic girdle is a complete bony ring, it provides more stable support but less mobility than the incomplete ring of the pectoral girdle. In addition, the pelvis in a woman protects a developing fetus and forms a passageway through which the fetus passes during delivery.

Ilium

The largest of the three hip bones is the ilium. The **iliac crest** forms the most superior border of the ilium (see figure 6.31). The crest ends anteriorly as the **anterior superior iliac spine** and posteriorly as the **posterior superior iliac spine.** The crest and anterior spine can be felt and even seen in thin individuals. The **greater sciatic** (sigh-AT-ik) **notch** is on the posterior side of the ilium, just

inferior to the posterior inferior iliac spine. The sciatic nerve passes through the greater sciatic notch. The **auricular surface** of the ilium joins the sacrum to form the **sacroiliac joint** (see figure 6.30). The medial side of the ilium consists of a large depression called the **iliac fossa.**

Ischium

Of the two inferior hip bones, the ischium is more posterior than the pubis. The ischium has a thick **ischial** (IS-kee-ul) **tuberosity.** Posterior thigh muscles attach to the ischial tuberosity and it's the portion of the pelvis on which a person sits (see figure 6.31*a*). The ischium also has a posterior **ischial spine,** a site of ligament attachment.

Pubis

The pubis forms the anterior portion of the pelvic girdle (see figure 6.31). The two pubic bones are joined by the **pubic symphysis** (SIM-fi-sis; joined), a thick pad of fibrocartilage. At the point of fusion with the ischium, the two bones surround the noticeable **obturator** (OB-tour-ate-or; closed up) **foramen** (see figure 6.31). However, in a living person, only a few nerves and blood vessels pass through; it is otherwise closed by a ligament.

The pelvis is subdivided into a **true pelvis** and a **false pelvis** (figure 6.32). The opening to the true pelvis is the **pelvic inlet,** and the inferior opening of the true pelvis is the **pelvic outlet.** The false pelvis is formed by muscle overlying bone of the true pelvis.

Figure 6.32 **Comparison of the Male Pelvis to the Female Pelvis**

(*a*) In a male, the pelvic inlet (*upper, red dashed line*) and outlet (*lower, blue dashed line*) are small, and the subpubic angle is less than 90 degrees. (*b*) In a female, the pelvic inlet (*upper, red dashed line*) and outlet (*lower, blue dashed line*) are larger,

and the subpubic angle is 90 degrees or greater. (*c*) A midsagittal section through the pelvis shows the pelvic inlet (*upper, red arrow* and *upper, red dashed line*) and the pelvic outlet (*lower, blue arrow* and *lower, blue dashed line*).

Comparison of the Male Pelvis and the Female Pelvis

The male pelvis is usually more massive than the female pelvis as a result of the greater weight and size of the male body. The female pelvis is broader and has a larger, more rounded pelvic inlet and outlet (table 6.3; figure 6.32*a*, *b*), consistent with the need to allow the fetus to pass through these openings in the female pelvis during childbirth. A wide, circular pelvic inlet and a pelvic outlet with widely spaced ischial spines can facilitate delivery of the newborn.

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Table 6.3 Differences Between Male and Female Pelvic Girdles

Area	Description of Difference
General	Female pelvis somewhat lighter in weight and wider laterally but shorter superiorly to inferiorly and less funnel-shaped; less obvious muscle attachment points in female than in male
Sacrum	Broader in female, with the inferior portion directed more posteriorly; the sacral promontory projects less anteriorly in female
Pelvic inlet	Heart-shaped in male; oval in female
Pelvic outlet	Broader and more shallow in female
Subpubic angle	Less than 90 degrees in male; 90 degrees or more in female
Ilium	More shallow and flared laterally in female
Ischial spines	Farther apart in female
Ischial tuberosities	Turned laterally in female and medially in male (not shown in figure 6.32)

Thigh: Femur

The thigh, like the arm, contains a single bone, the **femur.** The femur has a prominent, rounded **head,** where it articulates with the acetabulum. The femur also has a well-defined **neck.** Both the head and neck of the femur are located at an oblique angle to its shaft (figure 6.33). The proximal shaft exhibits two projections: a **greater trochanter** (TROH-kan-ter; runner) lateral to the neck and a smaller, **lesser trochanter** inferior and posterior to the neck. Both trochanters are attachment sites for muscles that fasten the hip to the thigh. The greater trochanter and its attached muscles form a bulge that can be seen as the widest part of the hips.

Figure 6.33 APR **Bones of the Thigh**

(*a*) Anterior and posterior view of the right femur. (*b*) Photo of anterior view of the right femur. (*c*) Anterior view of the patella. (b) Christine Eckel/McGraw-Hill Education

The femur articulates with the tibia to form the knee. There are two smooth rounded projections that rotate on the superior surface of the tibia when we bend our knee.

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The **patella,** or kneecap, is a large sesamoid bone located within the tendon of the quadriceps femoris muscle group, which is the major muscle group of the anterior thigh (figure 6.33*c*). The patella articulates with the patellar groove of the femur to create a smooth articular surface over the anterior distal end of the femur. The patella holds the tendon away from the distal end of the femur.

Leg: Tibia and Fibula

The leg is the part of the lower limb between the knee and the ankle. Like the forearm, it consists of two bones: (1) the medial **tibia** (TIB-ee-ah), or shinbone, and

(2) the lateral **fibula** (FIB-you-lah; figure 6.34). The tibia is the larger of the two and is the major weight-bearing bone of the leg.

Figure 6.34 APR **Bones of the Leg**

(*a*) Anterior view of the articulated right tibia and fibula bones. (*b*) Photo of the anterior view of the articulated right tibia and fibula bones.

(b) Christine Eckel/McGraw-Hill Education

The rounded condyles of the femur rest on flat condyles on the proximal end of the tibia. Just distal to the condyles of the tibia, on its anterior surface, is the easily felt **tibial tuberosity** (see figure 6.34). The tibial tuberosity is the point of attachment for the quadriceps femoris muscle group. The fibula does not articulate with the femur, but its **head** articulates with the proximal end of the tibia.

Ankle

The **ankle** consists of the distal ends of the tibia and fibula forming a partial socket that articulates with a bone of the foot (the talus) (figure 6.35). A prominence can be seen on each side of the ankle. These are the **medial malleolus** of the distal tibia and the **lateral malleolus** of the distal fibula.

Figure 6.35 APR **Bones of the Right Foot**

The medial longitudinal arch is formed by the calcaneus, the talus, the navicular, the cuneiforms, and three medial metatarsal bones. The lateral longitudinal arch is formed by the calcaneus, the cuboid, and two lateral metatarsal bones. The transverse arch is formed by the cuboid and the cuneiforms.

Foot: Tarsals, Metatarsals, and Phalanges

There are seven **tarsal** (TAR-sahl; foot) **bones** (see figure 6.35). The tarsal bones include: (1) the **talus** (TAY-lus; ankle), (2) the **calcaneus** (kal-KAY-nee-us; heel), (3) the **navicular** (nah-VIK-you-lar), (4–6) the medial, intermediate, and lateral **cuneiforms** (KYOO-nee-ih-forms), and (7) the **cuboid** (KYOO-boyd) (see figure

6.35). A mnemonic used for the tarsal bones is **T**iger **C**ub **N**eeds **MILC** (**T**alus, **C**alcaneus, **N**avicular, **M**edial cuneiform, **I**ntermediate cuneiform, **L**ateral cuneiform, and **C**uboid).

The **metatarsal bones** and **phalanges** of the foot are arranged in a manner very similar to that of the metacarpal bones and phalanges of the hand, with the great toe (**hallux**) comparable to the thumb (figure 6.35). Small sesamoid bones often form in the tendons of muscles attached to the great toe. The ball of the foot is the junction between the metatarsal bones and the phalanges.

There are three primary **arches** in the foot formed by the positions of the tarsal bones and metatarsal bones and held in place by ligaments. Two **longitudinal arches** extend from the heel to the ball of the foot, and a **transverse arch** extends across the foot. The transverse arch is located at the connection between the five metatarsals, the three cuneiforms, and the cuboid. The arches serve as an adjustable lever to assist in the two main functions of the foot: (1) to support the body in its upright position both while standing and in forward movement during walking and (2) to push the body forward during walking and to absorb shock when the foot contacts the ground. The arches function similarly to the springs of a car, allowing the foot to give and spring back (see section 6.12).

6.12 JOINTS

Learning Outcomes *After reading this section, you should be able to*

A. Describe the two systems for classifying joints.
B. Explain the structure of a fibrous joint.
C. List the three types of joints.
D. Give examples of each type of joint.
E. Give examples of cartilaginous joints.
F. Illustrate the structure of a synovial joint.
G. Explain the roles of the components of a synovial joint.
H. Classify synovial joints based on the shape of the bones in the joint.
I. Give an example of each type of synovial joint.
J. Demonstrate the difference between the following pairs of movements: flexion and extension; plantar flexion and dorsiflexion; abduction and adduction; supination and pronation; elevation and depression; protraction and retraction; opposition and reposition; inversion and eversion.

Joints, or *articulations,* are commonly named according to the bones or portions of bones that join together; for example, the temporomandibular joint is between the temporal bone and the mandible. Some joints are given the Greek or Latin equivalent of the common name, such as cubital (KYOO-bi-tal; cubit, elbow or forearm) joint for the elbow joint.

Joints are classified structurally as fibrous, cartilaginous, or synovial, according to the major connective tissue type that binds the bones together and whether a fluid-filled joint capsule is present. Joints can also be classified in functional categories according to their degree of motion as *synarthroses* (nonmovable joints), *amphiarthroses* (slightly movable joints), or *diarthroses* (freely movable joints). In

general, fibrous and cartilaginous joints have little or no movement, while synovial joints have considerable movement. Because this functional classification is somewhat limited, our discussions are based on the more precise structural classification scheme.

Fibrous Joints

Fibrous joints are the articulating surfaces of two bones united by fibrous connective tissue. They have no joint cavity and exhibit little or no movement. Joints in this group are further subdivided on the basis of structure as (1) sutures, (2) syndesmoses, or (3) gomphoses.

Sutures

Sutures (SOO-churs) are fibrous joints between the bones of the skull (see figure 6.13). In a newborn, some parts of the sutures are quite wide and are called **fontanels** (FON-tah-nels), or soft spots (figure 6.36). They allow flexibility in the skull during the birth process, as well as growth of the head after birth.

Figure 6.36 **Fetal Skull Showing Fontanels and Sutures**
(*a*) Lateral view of the fetal skull fontanels and sutures. (*b*) Superior view of the fetal skull fontanels and sutures.

Syndesmoses

Syndesmoses (SIN-des-MOH-seez) are fibrous joints in which the bones are separated by some distance and held together by ligaments. An example is the fibrous membrane connecting most of the distal parts of the radius and ulna.

Gomphoses

Gomphoses (gom-FOH-seez) consist of pegs fitted into sockets and held in place by ligaments. The joint between a tooth and its socket is a gomphosis.

Cartilaginous Joints

Cartilaginous joints hold two bones together by a pad of cartilage. Like fibrous joints, these joints exhibit little or no movement. Cartilaginous joints are subdivided on the basis of the type of cartilage as (1) synchondroses, which contain hyaline cartilage, and (2) symphyses, which contain fibrocartilage.

Synovial Joints

Synovial (sih-NOH-vee-al) **joints** contain synovial fluid and allow considerable movement between articulating bones (figure 6.37). These joints are anatomically more complex than fibrous and cartilaginous joints. Most joints that unite the bones of the appendicular skeleton are synovial joints, reflecting the far greater mobility of the appendicular skeleton compared with the axial skeleton.

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Figure 6.37 APR **General Structure of a Synovial Joint**

Synovial joints are highly movable connections between bones. A membrane-lined and fluid-filled cavity separates the bones.

The articular surfaces of bones within synovial joints are covered with a thin layer of hyaline cartilage called **articular cartilage.** The articular cartilage provides a smooth surface where the bones meet. In some synovial joints, a flat pad of fibrocartilage, called a **meniscus** (meh-NIS-kus; pl. menisci, crescent-shaped) is present. A meniscus is a type of articular disk that only partially spans the synovial

cavity such that there is an opening in the center. Joints with menisci include the knee and wrist. The meniscus helps adjust the connection between articulating bones, which improves joint stability and reduces wear on the articular cartilage.

The space around the articular surfaces of the bones in a synovial joint is called the **joint cavity** (figure 6.37). The joint cavity is filled with synovial fluid and surrounded by a **joint capsule.** The joint capsule helps hold the bones together while still allowing for movement. The joint capsule consists of two layers: an outer fibrous capsule and an inner synovial membrane.

The **fibrous capsule** is the outer layer of the joint capsule (figure 6.37). It consists of dense irregular connective tissue and is continuous with the fibrous layer of the periosteum that covers the bones united at the joint. Portions of the fibrous capsule may thicken, and the collagen fibers may become regularly arranged to form ligaments. In addition, ligaments and tendons may be present outside the fibrous capsule, thereby contributing to the strength and stability of the joint while limiting movement in some directions.

The **synovial membrane** is the inner layer of the joint capsule (figure 6.37). It lines the joint cavity, except over the articular cartilage and articular disks and is a thin, delicate membrane The membrane produces **synovial fluid,** a viscous lubricating film that covers the surfaces of a joint. Synovial fluid is a complex mixture of polysaccharides, proteins, lipids, and cells derived from serum (blood fluid) filtrate and secretions from the synovial cells. The major polysaccharide, hyaluronic acid, provides much of the slippery consistency and lubricating qualities of synovial fluid.

In certain synovial joints, such as the shoulder and knee, the synovial membrane extends as a pocket, or sac, called a **bursa** (BURR-sah; pocket; pl. bursae, BURR-see; figure 6.37). Bursae contain synovial fluid and provide a cushion between structures that would otherwise rub against each other, such as tendons rubbing on bones or other tendons. Other bursae extend along tendons for some distance, forming **tendon sheaths. Bursitis** (ber-SIGH-tis), inflammation of a bursa, may cause considerable pain around the joint and restrict movement.

Articular cartilage receives nourishment from blood vessels that are at the peripheral margin of the cartilage but do not actually penetrate the cartilage or enter the joint cavity. Because the cartilage does not contain blood vessels, nutrients and oxygen must diffuse from the surrounding vessels into the cartilage. Nerves do not enter the cartilage or joint cavity.

Types of Synovial Joints

Synovial joints are classified according to the shape of the adjoining articular surfaces. The six types of synovial joints are (1) plane, (2) saddle, (3) hinge, (4) pivot, (5) ball-and-socket, and (6) ellipsoid (figure 6.38 table 6.4). Movements at synovial joints are described as **uniaxial,** occurring around one axis; **biaxial,** occurring around two axes situated at right angles to each other; or **multiaxial,** occurring around several axes.

Figure 6.38 **Examples of Synovial Joints**

(*a*) The elbow joint is formed between the humerus, radius, and ulna. (*b*) The knee joint is formed between the femur and the tibia. (*c*) The shoulder joint is formed between the humerus and the scapula. (*d*) The hip joint is formed between the femur and the hip bone.

Table 6.4	Synovial Joints		
	Class and Example of Joint	**Bones Joined**	**Movement**

	Class and Example of Joint	Bones Joined	Movement
	Plane		
	Intervertebral	Between articular processes of adjacent vertebrae	Uniaxial; slight
	Acromioclavicular	Acromion process of scapula and clavicle	Uniaxial; slight
	Carpometacarpal	Carpals and metacarpals 2–5	Uniaxial; slight
	Costovertebral	Ribs and vertebrae	Uniaxial; slight
	Intercarpal	Between carpal bones	Uniaxial; slight
	Intermetatarsal	Between metatarsal bones	Uniaxial; slight
	Intertarsal	Between tarsal bones	Uniaxial; slight
	Sacroiliac	Between sacrum and hip bone (complex joint with several planes and synchondroses)	Uniaxial; slight
	Tarsometatarsal	Tarsal bones and metatarsal bones	Uniaxial; slight
	Saddle		
	Carpometacarpal pollicis	Carpal and metacarpal of thumb	Biaxial
	Sternoclavicular	Manubrium of sternum and clavicle	Multiaxial; slight
	Hinge		
	Cubital (elbow)	Humerus, ulna, and radius	Uniaxial
	Knee	Femur and tibia	Uniaxial
	Interphalangeal	Between phalanges	Uniaxial
	Talocrural (ankle)	Talus, tibia, and fibula	Multiaxial; one predominates
	Pivot		
	Atlantoaxial	Atlas and axis	Uniaxial rotation
	Proximal radioulnar	Radius and ulna	Uniaxial rotation
	Distal radioulnar	Radius and ulna	Uniaxial rotation

	Class and Example of Joint	Bones Joined	Movement
Ball-and-socket Glenohumeral	*Ball-and-Socket* Glenohumeral (shoulder) Hip	Scapula and humerus Hip bone and femur	Multiaxial Multiaxial
Ellipsoid Atlantooccipital	*Ellipsoid* Atlantooccipital Metacarpophalangeal (knuckles) Metatarsophalangeal (ball of foot) Radiocarpal (wrist) Temporomandibular	Atlas and occipital bone Metacarpal bones and phalanges Metatarsal bones and phalanges Radius and carpal bones Mandible and temporal bone	Biaxial Biaxial Biaxial Multiaxial Multiaxial; one predominates

A **plane joint,** or *gliding joint,* consists of two flat bone surfaces of about equal size between which a slight gliding motion can occur (figure 6.38; table 6.4). These joints are considered uniaxial because some rotation is also possible but is limited by ligaments and adjacent bone. Examples are the articular processes between vertebrae.

A **saddle joint** consists of two saddle-shaped articulating surfaces oriented at right angles to each other so that their complementary surfaces articulate (table 6.4). Saddle joints are biaxial joints. The carpometacarpal joint of the thumb is an example.

A **hinge joint** is a uniaxial joint in which a convex cylinder in one bone is applied to a corresponding concavity in the other bone (table 6.4). Examples include the elbow and knee joints.

A **pivot joint** is a uniaxial joint that restricts movement to rotation around a single axis (table 6.4). A pivot joint consists of a relatively cylindrical bony process that rotates within a ring composed partly of bone and partly of ligament. The articulation between the head of the radius and the proximal end of the ulna is an example. The articulation between the dens, a process on the axis, and the atlas is another example.

A **ball-and-socket joint** consists of a ball (head) at the end of one bone and a socket in an adjacent bone into which a portion of the ball fits (table 6.4). This type of joint is multiaxial, allowing a wide range of movement in almost any direction. Examples are the shoulder and hip joints.

An **ellipsoid joint** (condyloid joint) is a modified ball-and- socket joint (table 6.4). The articular surfaces are ellipsoid in shape, rather than spherical as in regular ball-and-socket joints. Ellipsoid joints are biaxial, because the shape of the joint

limits its range of movement almost to a hinge motion in two axes and restricts rotation. The atlantooccipital joint of the neck is an example.

Types of Movement

The types of movement occurring at a given joint are related to the structure of that joint. Some joints are limited to only one type of movement, whereas others permit movement in several directions. All the movements are described relative to the anatomical position. Because most movements are accompanied by movements in the opposite direction, they are often illustrated in pairs (figure 6.39).

Figure 6.39 APR **Types of Movement**

(*a*) Flexion and extension of the elbow. (*b*) Flexion and extension of the neck. (*c*) Abduction and adduction of the fingers. (*d*) Pronation and supination of the hand. (*e*) Medial and lateral rotation of the arm. (*f*) Circumduction of the arm.

(a, d–f) ©Eric Wise (b, c) Tamara Klein/McGraw-Hill Education

Flexion and extension are common opposing movements (figure 6.39). **Flexion** is a bending movement that *decreases* the angle of the joint to bring the articulating bones closer together. **Extension** is a straightening movement that *increases* the angle of the joint to extend the articulating bones. These bending and extending movements can easily be seen at the elbow and knee joints (figure 6.39*a*, *b*).

Hyperextension is usually defined as extension of a joint beyond 180 degrees (figure 6.39*b*). Hyperextension can be a normal movement, such as looking up at the stars, but it can also result in injury. For example, when a person attempts to break a fall by putting out a hand, the force of the fall can result in hyperextension of the wrist, resulting in a sprained joint or broken bone.

There are special cases of flexion when describing the movement of the foot. Movement of the foot toward the plantar surface, as when standing on the toes, is commonly called **plantar flexion;** movement of the foot toward the shin, as when walking on the heels, is called **dorsiflexion** (figure 6.39*a*, *b*).

Abduction (ab-DUK-shun; to take away) is movement away from the median or midsagittal plane; **adduction** (to bring together) is movement toward the median plane (figure 6.39*c*). Moving the legs away from the midline of the body, as in the outward movement of "jumping jacks," is abduction, and bringing the legs back together is adduction.

Pronation (proh-NAY-shun) and **supination** (soo-pih-NAY-shun) refer to the unique rotation of the forearm. They are best demonstrated with the elbow flexed at a 90-degree angle. When the elbow is flexed, pronation is rotation of the forearm so that the palm is down, and supination is rotation of the forearm so that the palm faces up (figure 6.39*d*).

Eversion (ee-VER-shun) is turning the foot so that the plantar surface (bottom of the foot) faces laterally; **inversion** (in-VER-shun) is turning the foot so that the plantar surface faces medially.

Rotation is the turning of a structure around its long axis, as in shaking the head "no." Rotation of the arm can best be demonstrated with the elbow flexed (figure 6.39*e*) so that rotation is not confused with supination and pronation of the forearm. With the elbow flexed, medial rotation of the arm brings the forearm against the anterior surface of the abdomen, and lateral rotation moves it away from the body.

Circumduction (ser-kum-DUK-shun) occurs at freely movable joints, such as the shoulder. In circumduction, the arm moves so that it traces a cone where the shoulder joint is at the cone's apex (figure 6.39*f*).

In addition to the movements pictured in figure 6.39, several other movement types have been identified:

- **Protraction** (proh-TRAK-shun) is a movement in which a structure, such as the mandible, glides anteriorly.
- In **retraction** (ree-TRAK-shun), the structure glides posteriorly.
- **Elevation** is movement of a structure in a superior direction. Closing the mouth involves elevation of the mandible.
- **Depression** is movement of a structure in an inferior direction. Opening the mouth involves depression of the mandible.
- **Excursion** is movement of a structure to one side, as in moving the mandible from side to side.
- **Opposition** is a movement unique to the thumb and little finger. It occurs when the tips of the thumb and little finger are brought toward each other

across the palm of the hand. The thumb can also oppose the other digits.

- **Reposition** returns the digits to the anatomical position.

Most movements that occur in the course of normal activities are combinations of movements. A complex movement can be described by naming the individual movements involved.

When the bones of a joint are forcefully pulled apart and the ligaments around the joint are pulled or torn, a *sprain* results. A *separation* exists when the bones remain apart after injury to a joint. A *dislocation* is when the end of one bone is pulled out of the socket in a ball-and-socket, ellipsoid, or pivot joint. Most dislocations result in stretching of the joint capsule. Once the joint capsule has been stretched by a dislocation, the joint may be predisposed to future dislocations. Some individuals have hereditary "loose" joints and are more likely to experience a dislocation.

Understand **Apply It 5**

What combination of movements at the shoulder and elbow joints allows a person to perform a crawl stroke in swimming?

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SYSTEMS PATHOLOGY

Osteoporosis

Background Information

Betty has been diagnosed with osteoporosis. Osteoporosis is one of several disorders of the skeletal system that can arise (table 6.5). Betty is 65 years old and is a heavy smoker. She also does not exercise, has a poor diet, and seldom goes outdoors. Osteoporosis involves many systems of the body (figure 6.40). Radiographs revealed significant loss of bone density (figure 6.41) and a fractured femur neck. **Osteoporosis,** or porous bone, is a loss of bone matrix. This loss of bone mass makes bones so porous and weakened that they become deformed and prone to fracture (see figure 6.42). The occurrence of osteoporosis increases with age. In both men and women (although it is 2.5 times more common in women), bone mass starts to decrease at about age 40 and continually decreases thereafter. Women can eventually lose approximately one-half, and men one-quarter, of their spongy bone.

Table 6.5 REPRESENTATIVE DISEASES AND DISORDERS: Skeletal System

Condition	Description
	SKELETAL DISORDERS
Growth and Developmental Disorders	
Gigantism	Abnormally increased body size due to excessive growth at the epiphyseal plates
Dwarfism	Abnormally small body size due to improper growth at the

	epiphyseal plates
Rickets	Growth retardation due to nutritional deficiencies in minerals (Ca^{2+}) or vitamin D; results in bones that are soft, weak, and easily fractured
Bacterial Infections	
Tuberculosis	Typically, a lung bacterium that can also affect bone
Decalcification	
Osteomalacia	Softening of adult bones due to calcium depletion; often caused by vitamin D deficiency
	JOINT DISORDERS
Arthritis	Inflammation of a joint; causes include infectious agents, metabolic disorders, trauma, and immune disorders
Rheumatoid arthritis	General connective tissue autoimmune disease
Gout	Increased production and accumulation of uric acid crystals in tissues, including joint capsules
Bursitis and bunions	
Bursitis	Inflammation of a bursa
Bunion	Most bunions are deformations of the first metatarsal (the great toe); bursitis may accompany this deformity; irritated by tight shoes

Figure 6.40 Interactions Among Organ Systems and Osteoporosis

Many body systems are involved in osteoporosis, as this diagram illustrates.

Figure 6.41 Bone Loss

Photomicrograph of osteoporotic bone and normal bone.

Michael Klein/Photolibrary/Getty Images

Figure 6.42 Fracture

Radiograph of a fractured hip.

Princess Margaret Rose Orthopaedic Hospital/SPL/Science Source

In women, decreased production of the female reproductive hormone estrogen can cause osteoporosis, mostly in spongy bone, especially in the vertebrae of the spine and the bones of the forearm. Collapse of the vertebrae can cause a decrease in height or, in more severe cases, kyphosis in the upper back (figure 6.43). Estrogen levels decrease as a result of menopause; removal of the ovaries; amenorrhea (lack of menstrual cycle) due to extreme exercise or anorexia nervosa (self-starvation); or cigarette smoking.

Figure 6.43 Vertebral Collapse

Osteoporosis can cause the vertebrae to collapse, which results in an outward bulge called kyphosis.

Bengt-Goran Carlsson/age fotostock

In men, reduction in testosterone levels can cause loss of bone tissue. However, this is less of a problem in men than in women because men have denser bones than women, and

testosterone levels generally don't decrease significantly until after age 65.

Inadequate dietary intake or absorption of calcium, sometimes due to certain medications, can also contribute to osteoporosis. Absorption of calcium from the small intestine decreases with age. Finally, too little exercise or disuse from injury can all cause osteoporosis. Significant amounts of bone are lost after only 8 weeks of immobilization.

Early diagnosis of osteoporosis can lead to more preventative treatments. Instruments that measure the absorption of photons (particles of light) by bone are currently used; of these, dual-energy x-ray absorptiometry (DEXA) is considered the best. Supplementation of dietary calcium and vitamin D and exercise are the best preventative and rehabilitory measures to prevent bone loss or regain mild bone loss. Calcitonin (Miacalcin) inhibits osteoclast activity, and alendronate (Fosamax), which binds to hydroxyapatite, also inhibits osteoclasts. Although osteoporosis is linked to estrogen loss, estrogen therapy has been associated with many side effects, including breast cancer, and is no longer recommended as a treatment.

Apply It 6

What advice should Betty give to her granddaughter so that the granddaughter will be less likely to develop osteoporosis when she is Betty's age?

EFFECTS OF AGING ON THE SK

The most significant age-related changes in the skeletal system affect the joints as well as the quality and quantity of bone matrix. The bone matrix in an older bone is more brittle than in a younger bone because decreased collagen production results in relatively more mineral and less collagen fibers. With aging, the amount of matrix also decreases because the rate of matrix formation by osteoblasts becomes slower than the rate of matrix breakdown by osteoclasts.

Significant loss of bone increases the likelihood of bone fractures. For example, loss of trabeculae greatly increases the risk of fractures of the vertebrae. In addition, loss of bone and the resulting fractures can cause deformity, loss of height, pain, and stiffness. Loss of bone from the jaws can also lead to tooth loss.

A number of changes occur within many joints as a person ages. Changes in synovial joints have the greatest effect and often present major problems for elderly people. With use, the cartilage covering articular surfaces can wear down and the rate of replacement declines. Many people also experience arthritis, an inflammatory degeneration of the joints, with advancing age. In addition, the ligaments and tendons

surrounding a joint shorten and become less flexible with age, resulting in decreased range of motion.

SUMMARY

The skeletal system consists of bone, cartilage, tendons, and ligaments.

6.1 Functions of the Skeletal System

1. The skeletal system provides the major support for the body.
2. Bone protects internal organs.
3. Joints allow movement between bones.
4. Bones store and release minerals as needed by the body.
5. Bone marrow gives rise to blood cells and platelets.

6.2 Bone Histology

Bone Matrix

1. Collagen provides flexible strength.
2. Hydroxyapatite provides compressional strength.

Bone Cells

1. Osteoblasts produce bone matrix and become osteocytes.
   - Osteoblasts connect to one another through cell extensions and surround themselves with bone matrix to become osteocytes.
   - Osteocytes are located in lacunae and are connected to one another through canaliculi.
2. Osteoclasts break down bone (with assistance from osteoblasts).
3. Osteoblasts originate from osteochondral progenitor cells, whereas osteoclasts originate from monocyte/macrophage lineage stem cells in red bone marrow.

Spongy and Compact Bone

1. Spongy bone has many spaces.
   - Lamellae combine to form trabeculae, beams of bone that inter-connect to form a lattice-like structure with spaces filled with bone marrow and blood vessels.
   - The trabeculae provide structural strength.
2. Compact bone is dense, with few spaces.

- Compact bone consists of organized lamellae: lamellae surround central canals, forming osteons;
- Canals within compact bone provide a means for exchanging gases, nutrients, and waste products. From the periosteum or endosteum, perforating canals carry blood vessels to central canals, and canaliculi connect central canals to osteocytes.

6.3 Bone Anatomy

Structure of a Long Bone

1. The diaphysis is the shaft of a long bone, and the epiphyses are distinct from the diaphysis and house the epiphyseal plate.
2. The epiphyseal plate is the site of lengthwise bone growth.
3. The medullary cavity is a space within the diaphysis.
4. Red marrow is the site of blood cell production, and yellow marrow consists of fat.
5. The periosteum covers the outer surface of bone.
   - The outer layer contains blood vessels and nerves.
   - The inner layer contains osteoblasts and osteoclasts.
   - Perforating fibers hold the periosteum, ligaments, and tendons in place.
6. The endosteum lines cavities inside bone and contains osteoblasts and osteoclasts.

6.4 Bone Development

1. Intramembranous ossification occurs within connective tissue membranes.
2. Endochondral ossification occurs within cartilage.

6.5 Bone Growth

Bone elongation occurs at the epiphyseal plate as chondrocytes proliferate, enlarge, die, and are replaced by bone.

6.6 Bone Remodeling

Bone remodeling consists of removal of existing bone by osteoclasts and deposition of new bone by osteoblasts.

6.7 Bone Repair

During bone repair, cells move into the damaged area and form a callus, which is replaced by bone.

6.8 Calcium Homeostasis

1. Osteoclasts remove calcium from bone, causing blood calcium levels to increase.

2. Osteoblasts deposit calcium into bone, causing blood calcium levels to decrease.
3. Parathyroid hormone increases bone breakdown, whereas calcitonin decreases bone breakdown.

6.9 Skeletal Anatomy Overview

Bones have processes, smooth surfaces, and holes that are associated with ligaments, muscles, joints, nerves, and blood vessels.

6.10 Axial Skeleton

The axial skeleton consists of the skull, auditory ossicles, hyoid bone, vertebral column, and thoracic cage.

Skull

1. The skull, or cranium, can be thought of as a single unit.
2. The parietal bones are joined at the midline by the sagittal suture; they are joined to the frontal bone by the coronal suture, to the occipital bone by the lambdoid suture, and to the temporal bone by the squamous suture.
3. Nuchal lines are the points of attachment for neck muscles.
4. The skull is composed of 22 bones.
   - The auditory ossicles, which function in hearing, are located inside the temporal bones.
   - The cranial bone protects the brain.
   - The facial bones protect the sensory organs of the head and are muscle attachment sites (mastication, facial expression, and eye muscles).
   - The mandible and maxillae possess alveolar processes with sockets for the attachment of the teeth.
5. Frontal Bone
   - The orbits contain the eyes.
6. Parietal Bones
   - The temporal lines are attachment points of the temporalis muscle.
7. Temporal Bones
   - The external auditory canal transmits sound waves toward the eardrum.
   - Important neck muscles attach to the mastoid process.
   - The zygomatic arch, from the temporal and zygomatic bones, forms a bridge across the side of the skull.
   - The mandible articulates with the temporal bone.

- Blood reaches the brain through the internal carotid arteries, which pass through the carotid canals, and through the vertebral arteries, which pass through the foramen magnum.
- Most blood leaves the brain through the internal jugular veins, which exit through the jugular foramina.
- Styloid processes provide attachment points for three muscles involved in moving the tongue, hyoid bone, and pharynx.

8. Occipital Bone
   - The spinal cord and brain are connected through the foramen magnum.
   - Occipital condyles are points of articulation between the skull and the vertebral column.
9. Sphenoid Bone
   - Sinuses within bone are air-filled cavities. The paranasal sinuses, which connect to the nasal cavity, are the frontal, sphenoidal, and maxillary sinuses and the ethmoidal labyrinth.
   - The sella turcica is occupied by the pituitary gland.
10. Ethmoid Bone
    - The nasal cavity is divided by the nasal septum, and the hard palate separates the nasal cavity from the oral cavity.
    - The crista galli is a point of attachment for one of the meninges.
    - The olfactory nerves extend into the roof of the nasal cavity through the cribriform plate.

Hyoid Bone

The hyoid bone, which is not attached to other bones, is the attachment site for the throat and tongue muscles.

Vertebral Column

1. The vertebral column contains 7 cervical, 12 thoracic, and 5 lumbar vertebrae, plus 1 sacral bone and 1 coccyx bone.
2. Each vertebra consists of a body, an arch, and processes.
3. Regional differences in vertebrae are as follows: Cervical vertebrae have transverse foramina; thoracic vertebrae have long spinous processes and attachment sites for the ribs; lumbar vertebrae have rectangular transverse and spinous processes, and the position of their facets limits rotation; the sacrum is a single, fused bone; the coccyx is 4 or fewer fused vertebrae.

Thoracic Cage

1. The rib cage consists of the thoracic vertebrae, the ribs, and the sternum.

2. There are 12 pairs of ribs: 7 true and 5 false (2 of the false ribs are also called floating ribs).
3. The sternum consists of the manubrium, the body, and the xiphoid process.

6.11 Appendicular Skeleton

The appendicular skeleton consists of the bones of the upper and lower limbs and their girdles.

Pectoral Girdle

The pectoral girdle includes the scapulae and clavicles.

Upper Limb

The upper limb consists of the arm (humerus), forearm (ulna and radius), wrist (8 carpal bones), and hand (5 metacarpal bones, 3 phalanges in each finger, and 2 phalanges in the thumb).

Pelvic Girdle

The pelvic girdle is made up of the 2 hip bones. Each hip bone consists of an ilium, an ischium, and a pubis. The hip bones, sacrum, and coccyx form the pelvis.

Lower Limb

The lower limb includes the thigh (femur), leg (tibia and fibula), ankle (7 tarsal bones), and foot (metatarsal bones and phalanges, similar to the bones in the hand).

6.12 Joints

A joint is a place where bones come together.

Fibrous Joints

Fibrous joints consist of bones united by fibrous connective tissue.
They allow little or no movement.

Cartilaginous Joints

Cartilaginous joints consist of bones united by cartilage, and they exhibit slight movement.

Synovial Joints

1. Synovial joints are capable of considerable movement. They consist of the following:
   - Articular cartilage on the ends of bones that provides a smooth surface for articulation. Articular disks can provide additional support.
   - A joint cavity is surrounded by a joint capsule of fibrous connective tissue, which holds the bones together while permitting flexibility. A synovial membrane produces

synovial fluid, which lubricates the joint.

2. Bursae are extensions of synovial joint cavities that protect skin, tendons, or bone from structures that could rub against them.
3. Synovial joints are classified according to the shape of the adjoining articular surfaces: plane (two flat surfaces), saddle (two saddle-shaped surfaces), hinge (concave and convex surfaces), pivot (cylindrical projection inside a ring), ball-and-socket (rounded surface into a socket), and ellipsoid (ellipsoid concave and convex surfaces).

Types of Movement

The major types of movement are flexion/extension, abduction/adduction, pronation/supination, eversion/inversion, rotation, circumduction, protraction/retraction, elevation/depression, excursion, and opposition/reposition.

REMEMBERING AND UNDERSTANDING

1. What are the primary functions of the skeletal system?
2. Name the major types of fibers and molecules in the extracellular matrix of the skeletal system. How do they contribute to the functions of tendons, ligaments, cartilage, and bones?
3. Define diaphysis, epiphysis, epiphyseal plate, medullary cavity, articular cartilage, periosteum, and endosteum.
4. Describe the structure of compact bone. How do nutrients reach the osteocytes in compact bone?
5. Describe the structure of spongy bone. What are trabeculae? How do nutrients reach osteocytes in trabeculae?
6. Define and describe intramembranous and endochondral ossification.
7. How do bones grow in diameter? How do long bones grow in length?
8. What is accomplished by bone remodeling? How does bone repair occur?
9. Define the axial skeleton and the appendicular skeleton.
10. Name the bones of the braincase and the face.
11. Give the locations of the paranasal sinuses. What are their functions?

12. What is the function of the hard palate?
13. Through what foramen does the brain connect to the spinal cord?
14. How do the vertebrae protect the spinal cord? Where do spinal nerves exit the vertebral column?
15. Name and give the number of each type of vertebra. Describe the characteristics that distinguish the different types of vertebrae from one another.
16. What is the function of the thoracic cage? Name the parts of the sternum. Distinguish among true, false, and floating ribs.
17. Name the bones that make up the pectoral girdle, arm, forearm, wrist, and hand. How many phalanges are in each finger and in the thumb?
18. Define the pelvic girdle. What bones fuse to form each hip bone? Where and with what bones do the hip bones articulate?
19. Name the bones of the thigh, leg, ankle, and foot.
20. Define joint, or articulation. Name and describe the differences among the three major classes of joints.
21. Describe the structure of a synovial joint. How do the different parts of the joint permit joint movement?
22. On what basis are synovial joints classified? Describe the different types of synovial joints, and give examples of each. What movements does each type of joint allow?
23. Describe and give examples of flexion/extension, abduction/adduction, and supination/pronation.

CRITICAL THINKING

1. A 12-year-old boy fell while playing basketball. The physician explained that the head (epiphysis) of the femur was separated from the shaft (diaphysis). Although the bone was set properly, by the time the boy was 16, it was apparent that the injured lower limb was shorter than the normal one. Explain why this difference occurred.
2. Justin leaped from his hotel room to avoid burning to death in a fire. If he landed on his heels, what bone was likely to fracture? Unfortunately for Justin, an iron beam fell on the distal part of Justin's foot (not the toes). What bones now could be fractured?
3. One day while shopping, LaShaya picked up her 3-year-old son, Samuel, by his right wrist and lifted him into a shopping cart. She heard a clicking sound, and Samuel immediately began to cry and hold his elbow. Given that lifting the child caused a

separation at the elbow, which is more likely: separation of the radius and humerus, or separation of the ulna and humerus?

4. Why are women knock-kneed more commonly than men?
5. Explain why running helps prevent osteoporosis in the elderly. Does the benefit include all bones or mainly those of the lower limbs and spine?
6. A patient has been diagnosed with hyperparathyroidism. Describe the patient's blood Ca^{2+} levels. What would you expect to happen to the patient's bone density?

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

7

Muscular System

Muscles control movement of our bodies. You will learn that even very rapid movements, such as the blink of an eye, require a complex series of events. We will quickly move from considering whole muscles to studying one small portion of the membrane of one muscle cell. When you've completed this chapter, you will have a better understanding of muscle contraction and the muscles that perform the contractions.

LEARN TO APPLY IT

Anthony decided to change his normal lifting routine to increase the number of repetitions (reps) of each weight. He was surprised when he became fatigued much more quickly than normal. In fact, his muscles became so weak that he could not continue exercising that particular muscle group. Using figures 7.9 and 7.10, answer the following questions.

Apply **a. Why did Anthony's muscles fatigue when lifting the same weight as normal, but for more reps in a row?**

Apply **b. What would be the Ca^{2+} level in the sarcoplasmic reticulum of his muscle after lifting many reps compared to lifting each weight once?**

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

7.1 FUNCTIONS OF THE MUSCULAR SYSTEM

Learning Outcome *After reading this section, you should be able to*

A. List the functions of the muscular system.

A runner rounds the last corner of the track and sprints for the finish line. Her arms and legs are pumping as she tries to reach her maximum speed. Her heart is beating rapidly, and her breathing is rapid, deep, and regular. Blood is shunted away from her digestive organs, and a greater volume is delivered to her skeletal muscles to maximize their oxygen supply. These actions are accomplished by muscle tissue, the most abundant tissue of the body and one of the most adaptable.

You don't have to be running for the muscular system to be at work. Even when you aren't consciously moving, postural muscles keep you sitting or standing upright, respiratory muscles keep you breathing, the heart continuously pumps blood to all parts of your body, and blood vessels constrict or relax to direct blood to organs where it is needed.

In fact, movement within the body is accomplished in various ways: by cilia or flagella on the surface of certain cells, by the force of gravity, or by the contraction of muscles. But most of the body's movement results from muscle contraction. As described in chapter 4, there are three types of muscle tissue: (1) skeletal, (2) cardiac, and (3) smooth (figure 7.1; Table 7.1). This chapter focuses primarily on the structure and function of skeletal muscle; cardiac and smooth muscle are described only briefly. Following are the major functions of the muscular system:

1. *Movement of the body.* Contraction of skeletal muscles is responsible for the overall movements of the body, such as walking, running, and manipulating objects with the hands.
2. *Maintenance of posture.* Skeletal muscles constantly maintain tone, which keeps us sitting or standing erect.
3. *Respiration.* Contraction of the skeletal muscles of the thoracic cage, as well as the diaphragm, helps us breathe.
4. *Production of body heat.* When skeletal muscles contract, heat is given off as a by-product. This released heat is critical to the maintenance of body temperature.
5. *Communication.* Skeletal muscles are involved in all aspects of communication, including speaking, writing, typing, gesturing, and facial expressions.
6. *Constriction of organs and vessels.* The contraction of smooth muscle within the walls of internal organs and vessels causes those structures to constrict. This constriction can help propel and mix food and water in the digestive tract, propel secretions from organs, and regulate blood flow through vessels.
7. *Contraction of the heart.* The contraction of cardiac muscle causes the heart to beat, propelling blood to all parts of the body.

Figure 7.1 **Overview of the Muscular System**

There are three types of muscle tissue comprising the muscular system: skeletal, cardiac, and smooth muscle.

TABLE 7.1 Comparison of Muscle Types APR

	Skeletal Muscle	Smooth Muscle	Cardiac Muscle
Location	Attached to bones	Walls of hollow organs, blood vessels, and glands	Heart
Appearance			
Cell Shape	Long, cylindrical	Spindle-shaped	Branched, cylindrical
Nucleus	Multiple, peripherally located	Single, centrally located	Single, centrally located

	Skeletal Muscle	Smooth Muscle	Cardiac Muscle
Special Cell-to-Cell Attachments	None	Gap junctions join some smooth muscle cells together	Intercalated disks
Striations	Yes	No	Yes
Autorhythmic	No	Yes (some smooth muscle)	Yes
Control	Voluntary and involuntary (reflexes)	Involuntary	Involuntary
Function	Body movements	Moving food through the digestive tract, emptying the urinary bladder, regulating the blood vessel diameter, contracting many gland ducts	Pumping blood; contractions provide the major force for propelling blood through blood vessels

7.2 GENERAL PROPERTIES OF MUSCLE TISSUE

Learning Outcome *After reading this section, you should be able to*

A. Explain the four functional properties of muscle tissue.

Muscle tissue is highly specialized. It has four major functional characteristics:

1. **Contractility** (kon-trak-TIL-i-tee) is the ability of muscle to shorten forcefully, or contract. Skeletal muscle contraction causes the structures to which they are attached (such as a bone) to move. Smooth muscle contraction increases pressure inside hollow organs, such as the intestines. Cardiac muscle contraction increases pressure inside the heart. On the other hand, muscles can lengthen passively. Forces that oppose contraction cause muscle to lengthen. Examples of these types of forces include gravity pulling on a limb and the pressure of fluid in a hollow organ, such as urine in the bladder. Thus muscle shortening is forceful and muscle lengthening is passive.
2. **Excitability** (ek-SIGH-tah-BIL-i-tee) is the capacity of muscle to respond to a stimulus. For skeletal muscle, the stimulus to contract is from nerves that we consciously control. Smooth and cardiac muscle fibers contract spontaneously, but also receive involuntary neural signals and hormonal signals to modulate force or rate of contraction.
3. **Extensibility** (eks-TEN-si-BIL-i-tee) means that a muscle can be stretched beyond its normal resting length and still be able to contract. If you stretch to reach a dropped pencil, your muscles are longer than they are normally, but you can still retrieve the pencil.
4. **Elasticity** (ee-lass-TISS-i-tee) is the ability of muscle to recoil to its original resting length after it has been stretched.

7.3 SKELETAL MUSCLE ANATOMY

Learning Outcomes *After reading this section, you should be able to*

A. Describe the connective tissue components of skeletal muscle.
B. Explain the blood supply and innervation of skeletal muscle.
C. Discuss the origin of muscle fibers and explain how muscle hypertrophy occurs.
D. Describe the components of a muscle fiber.
E. Relate the types of myofilaments and describe their structures.
F. Produce diagrams that illustrate the arrangement of myofilaments in a sarcomere.
G. Describe how the sliding filament model explains the contraction of muscle fibers.
H. Explain what happens to the length of the A band, I band, and H zone during contraction.

Whole Skeletal Muscle Anatomy

Skeletal muscle with its associated connective tissue, constitutes approximately 40% of body weight. Skeletal muscle is so named because many of the muscles are attached to the skeletal system. However, some skeletal muscle attaches to the skin or connective tissue sheets. Skeletal muscle is also called *striated muscle* because transverse bands, or striations, can be seen in the muscle under the microscope.

Individual skeletal muscles, such as the biceps brachii, are complete organs. Recall from chapter 1 that an organ consists of two or more tissue types working together for a common function. A skeletal muscle consists of skeletal muscle tissue, nervous tissue, connective tissue, and adipose tissue. For our purposes, we will start our discussion of skeletal muscle anatomy and physiology at the whole muscle (organ) level and conclude at the cellular level. Each muscle cell is called a **muscle fiber.**

Connective Tissue Coverings

Each skeletal muscle is surrounded by several connective tissue layers that support the muscle during contraction. A skeletal muscle has three layers of connective tissue: (1) the epimysium, (2) the perimysium, and (3) the endomysium.

The **epimysium** (ep-ih-MIS-ee-um; *mys*, muscle) forms a connective tissue sheath that surrounds each skeletal muscle. The protein fibers of the epimysium gradually merge with a layer of connective tissue between adjacent muscles and connecting the skin to superficial muscles. These outer layers of connective tissue separate the muscles from nearby structures.

The **perimysium** (PER-i-MIS-ee-um, PER-i-MIZ-ee-um) subdivides each whole muscle into numerous, visible bundles of muscle fibers (cells) called **fascicles** (FAS-i-kuhls). The perimysium is a loose connective tissue serving as passageways for blood vessels and nerves that supply each fascicle.

The **endomysium** (EN-doh-MIS-ee-um) is a delicate layer of connective tissue that separates the individual muscle fibers within each fascicle. The endomysium serves as passageways for nerve fibers and blood vessels that supply each separate muscle fiber.

The protein fibers of the three layers of connective tissue blend into one another and merge at the ends of most muscles to form **tendons,** which attach muscle to bone.

Skeletal Muscle Fiber Anatomy

Skeletal muscle fibers are very unique cells. They are enormous cells with several hundred nuclei just under the cell membrane. Most skeletal muscle fibers range in size from about 1 millimeter (mm) to about 4 centimeters (cm) in length, but some skeletal muscle fibers are as much as 30 cm (almost 1 foot) in length. Large muscles contain many large-diameter muscle fibers, whereas small, delicate muscles contain many small-diameter muscle fibers. However, most muscles contain a mixture of small- and large-diameter muscle fibers. As seen in a longitudinal section, alternating light and dark bands give the muscle fiber a **striated** (STRI-ate-ed; banded), or striped, appearance (Table 7.1). The number of skeletal muscle fibers remains relatively constant after birth. Enlargement of muscles results from an increase in the *size* of each muscle fiber, not from an increase in the *number* of muscle fibers. In the same way, enlargement of muscles due to exercise is mostly because of an increase in muscle fiber size, rather than an increase in number.

Histology of Muscle Fibers

Muscle contraction is much easier to understand when we consider the structure of a muscle fiber (figure 7.2). There are two main aspects to muscle contraction: (1) an electrical component and (2) a mechanical component. The parts of a skeletal muscle fiber can be categorized based on their specific role in muscle contraction.

Figure 7.2 APR **Structure of a Muscle**

(*a*) Organization of skeletal muscle components. A whole muscle is surrounded by a connective tissue sheath called epimysium. Each muscle is composed of muscle fascicles, each of which is surrounded by a connective tissue layer called perimysium. The fascicles are composed of individual muscle fibers (cells). Each fiber is surrounded by a connective tissue layer called endomysium. Muscle fibers contain groups of protein fibers, called myofibrils. Myofibrils are composed of protein filaments, called myofilaments. (*b*) Enlargement of one muscle fiber containing several myofibrils. The sarcoplasmic reticulum has enlarged sacs called terminal cisternae. Two terminal cisternae lie on either side of inward extensions of the sarcolemma called T tubules. The two terminal cisternae plus the T tubule form a triad.

Electrical Component Structures

Recall from section 7.2 that excitability is one of the four major functional properties of skeletal muscle. There are three muscle fiber components that respond to and transmit electrical signals: (1) the sarcolemma, (2) the transverse tubules, and (3) the sarcoplasmic reticulum.

1. The **sarcolemma** (SAR-koh-LEM-ah; *sarco*, flesh + *lemma*, husk; figure 7.2) is the cell membrane of muscle fibers. We will discuss its specific role in transmitting electrical impulses to the interior of the muscle fiber in section 7.4.
2. **Transverse tubules,** or **T tubules,** are tubelike inward folds of the sarcolemma (see figure 7.2). At regular intervals along the muscle fiber, the sarcolemma forms T tubules by projecting and extending into the interior of the muscle fiber. The T tubules carry electrical impulses into the center of the muscle fiber so that the muscle fiber contracts as a whole.
3. The **sarcoplasmic reticulum** (SAR-koh-PLAZ-mik re-TIK-you-lum) is a highly specialized smooth endoplasmic reticulum in skeletal muscle fibers that stores high levels of Ca^{2+} (see figure 7.2). Release of

Ca^{2+} from the sarcoplasmic reticulum is a "switch" for muscle contraction. T tubules lie next to enlarged portions of the sarcoplasmic reticulum called **terminal cisternae** (sis-TER-nee). Two terminal cisternae and their associated T tubule form a critical structure for muscle contraction called a **triad** (TRY-ad). We will continue our discussion of the triad in section 7.4. Muscle fibers contain other organelles, such as numerous mitochondria, as well as energy-storing glycogen granules. Together these organelles constitute the cytoplasm, called the **sarcoplasm** (SAR-koh-plazm) in muscle fibers.

Mechanical Component Structures

The general muscle property of contractility is due to two main structures in muscle fibers: (1) myofibrils and (2) myofilaments.

1. **Myofibrils** (my-oh-FIE-brillz) are bundles of protein filaments (see figure 7.2, 7.3). Each muscle fiber has numerous myofibrils in its sarcoplasm. The myofibrils are long threadlike structures that extend the entire length of the muscle fiber. The diameter of each myofibril is approximately one-sixth that of a human hair. It is the protein filaments in the myofibrils that interact to shorten the muscle fiber during contraction.
2. There are two types of **myofilaments** (my-oh-FIL-ah-ments) in each myofibril: (a) **actin** (AK-tin) **myofilaments,** or *thin filaments* and (b) **myosin** (MY-oh-sin) **myofilaments,** or *thick filaments* (figure 7.3). The actin and myosin myofilaments are arranged into highly ordered units called **sarcomeres** (SAR-koh-meerz; see figure 7.3). The sarcomeres are the structural and functional units of skeletal muscles. The myofilaments in the sarcomere provide the mechanical aspect of muscle contraction.

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Figure 7.3 APR **Skeletal Muscle Fiber**

(*a*) Electron micrograph of skeletal muscle, showing several sarcomeres in a muscle fiber. (*b*) Diagram of two adjacent sarcomeres. A sarcomere is mainly composed of actin myofilaments and myosin myofilaments. The Z disks anchor the actin myofilaments, and the M line holds the myosin myofilaments in place. (*c*) Actin myofilaments are composed of actin (shown as chains of purple spheres), tropomyosin (shown as long, blue strands lying along the actin), and troponin (shown as small red spheres with rod). (*d*) Myosin myofilaments are made up of many golf-club-shaped myosin molecules, with the heads pointing in one direction at one end and in the opposite direction at the other end.

(a) SPL/Getty Images

Sarcomeres

Sarcomeres join end to end, forming the myofibrils. The sarcomere is the smallest portion of a muscle that can contract. Each sarcomere has a precise boundary. Structures called **Z disks** form a stationary anchor for actin myofilaments (see figure 7.3). One sarcomere extends from one Z disk to the next Z disk. It is the arrangement of the actin and myosin myofilaments within sarcomeres that gives skeletal muscle its striated appearance.

Each sarcomere has three regions: (1) two lighter-staining regions, called I **bands** and (2) a central darker-staining region, called an A band. Each of the two I bands includes a Z disk and extend to the ends of the myosin myofilaments. The I bands contain only actin myofilaments (thin filaments) and thus appear lighter staining.

The darker-staining band in the center of each sarcomere is called an **A band.** Each A band contains both actin and myosin myofilaments overlapping, except in the center of the A band. The center of each A band has a smaller band, called the **H zone,** and contains only myosin myofilaments (thick filaments). The middle of each H zone has a dark line, called the **M line.** The M line consists of delicate protein filaments that hold the myosin myofilaments in place (see figure 7.3). The numerous myofibrils are oriented within each muscle fiber so that A bands and I bands of parallel myofibrils are aligned and thus produce the striated pattern seen through a microscope. Build a sarcomere using uncooked spaghetti noodles and uncooked angel hair noodles. Which is the actin and which is the myosin?

Actin and Myosin Myofilament Structure

Actin Myofilaments

Each actin myofilament is composed of three separate proteins: (1) actin, (2) tropomyosin, and (3) troponin (see figure 7.3). Each actin has an attachment site for the myosin myofilaments during muscle contraction. In a sense, we can think of the attachment sites on the actin as receptor sites for a portion of the myosin myofilament, the myosin head.

1. **Tropomyosin** (troh-poh-MY-oh-sin) is a long, fibrous protein that lies in the groove along the fibrous actin strand. In a relaxed muscle, tropomyosin is covering the attachment sites on the actin. A muscle cannot contract until the tropomyosin moves to uncover the active sites.
2. **Troponin** (TROH-poh-nin) consists of three subunits: (a) a subunit that anchors the troponin to the actin, (b) a subunit that prevents the tropomyosin from uncovering the actin attachment sites in a relaxed muscle, and (c) a subunit that binds Ca^{2+}.

It is the relationship among troponin and tropomyosin that determines when the skeletal muscle will contract. We will describe the specific process in section 7.4.

Myosin Myofilaments

Myosin myofilaments are composed of many elongated **myosin molecules** shaped like golf clubs (figure 7.3). Each myosin molecule consists of a **rod portion** lying parallel to the myosin myofilament and two **myosin heads** that extend laterally (figure 7.3). The myosin heads have three important properties: (1) The heads bind to active sites on the actin molecules to form **cross-bridges** to contract the muscle; (2) the heads are attached to the rod portion by a hinge region that bends and straightens during contraction; and (3) the heads break down adenosine triphosphate (ATP), releasing energy. Part of the energy is used to bend the hinge region of the myosin molecule during contraction.

Neuromuscular Junction Structure

Recall that each muscle fiber is in contact with a branch of a motor neuron axon from the brain or spinal cord. The motor neurons carry electrical signals called action potentials, which cause action potentials in the muscle fiber, followed by muscle contraction. The point of contact of motor neuron axon branches with the muscle fiber is called the **neuromuscular junction,** or **synapse** (figure 7.4). The neuromuscular junction consists of a group of enlarged axon terminals that rests on a portion of the sarcolemma. Therefore, a neuromuscular junction consists of (1) the axon terminals and (2) the area of the muscle fiber sarcolemma they innervate. Each axon terminal is called the **presynaptic** (PREE-si-NAP-tik) **terminal.** The space between the presynaptic terminal and the muscle fiber is the **synaptic** (si-NAP-tik) **cleft.** The muscle cell membrane in the area of the junction is called the **motor end-plate,** or the **postsynaptic** (post-si-NAP-tik) **membrane** (figure 7.4). Each presynaptic terminal contains numerous mitochondria and many small, spherical sacs, called **synaptic vesicles.** The synaptic vesicles contain the neurotransmitter **acetylcholine** (AS-eh-til-KOH-leen; **ACh**). A **neurotransmitter** (NYUR-oh-trans-MIT-er) is a molecule that allows a neuron to communicate with its target. They are released from a presynaptic membrane and diffuse across the synaptic cleft to alter the activity of the muscle fiber. Neurotransmitters can stimulate or inhibit the production of an action potential in the motor end-plate (the sarcolemma) by binding to **ligand-gated ion channels.** Recall from chapter 3 that gated ion channels limit ion movement across the cell membrane by opening and closing. Ligand-gated ion channels are specialized membrane transport proteins that are opened or closed by specific molecules, such as neurotransmitters. The generic term for these specific molecules is **ligand** (LIG-and, LIH-gand). When opened, the ligand-gated ion channels allow ions to cross the cell membrane (see section 7.4).

Figure 7.4 APR **Neuromuscular Junction**

(*a*) In a neuromuscular junction, several branches of an axon junction with a single muscle fiber. (*b*) Photomicrograph of a neuromuscular junction.

(b) Ed Reschke/Photolibrary/Getty Images

Sliding Filament Model

The primary function of skeletal muscle cells is to generate force by contracting, or shortening. The parallel arrangement of myofilaments in a sarcomere allows them to interact, which causes muscle contraction. This interaction is described by the **sliding filament model** (figure 7.5).

(a) **Relaxed sarcomere**

In a relaxed muscle, the actin and myosin myofilaments overlap slightly, and the H zone is visible. The sarcomere length is at its normal resting length. As a muscle contraction is initiated, actin myofilaments slide past the myosin myofilaments. The sliding of the myofilaments brings the Z disks closer together. The sarcomere begins to shorten.

(b) **Fully contracted sarcomere**

In a contracted muscle, the A bands, which are equal to the length of the myosin myofilaments, do not narrow because the length of the myosin myofilaments does not change, nor does the length of the actin myofilaments. In addition, the ends of the actin myofilaments are pulled to and overlap in the center of the sarcomere, shortening it, and the H zone is no longer visible.

Figure 7.5 APR **Sarcomere Shortening**

(*a*) In a relaxed sarcomere, the H zone is clearly visible. (*b*) In a contracted sarcomere, the H zone is no longer visible.

(a) Don W. Fawcett/Science Source (b) Biophoto Associates/Science Source

When a muscle contracts, the actin and myosin myofilaments in the sarcomere slide past one another and shorten the sarcomere. However, the myofilaments remain the same length as when the muscle is at rest. Shortening the sarcomeres also shortens the myofibrils. Because the myofibrils consist of sarcomeres joined end to end, their shortening causes the entire muscle fiber to shorten. Groups of muscle fibers make up a muscle fascicle, and several muscle fascicles make up a whole muscle. Therefore, when sarcomeres shorten, myofibrils, muscle fibers, muscle fascicles, and muscles all shorten to produce muscle contraction. On the other hand, during muscle relaxation, sarcomeres lengthen. This happens when an external force is applied to the muscle either by other muscles or by gravity. For example, muscle contraction causes a joint, such as the elbow or knee, to flex. Extension of the joint and lengthening of the muscle result from the contraction of muscles that produce the opposite movement. However, knowing the mechanism by which muscles shorten

is a small step toward understanding muscle contraction. What stimulates the sarcomeres to shorten in the first place? In order to fully understand muscle contraction, we must first consider the electrical properties of skeletal muscle fibers.

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7.4 SKELETAL MUSCLE FIBER PHYSIOLOGY

Learning Outcomes *After reading this section, you should be able to*

A. Describe the resting membrane potential and how it is generated and maintained.
B. Explain the role of ion channels in the production of an action potential.
C. Discuss the production of an action potential, including depolarization and repolarization.
D. State the all-or-none principle as it pertains to action potentials.
E. Describe the structure of a neuromuscular junction and explain how an action potential is transmitted across the junction.
F. Explain the events of excitation-contraction coupling.
G. Summarize the events of cross-bridge movement and relate them to muscle contraction.
H. State the conditions needed for muscle relaxation.

Excitability of Muscle Fibers

Recall the two main aspects of muscle fiber contraction: (1) the electrical component and (2) the mechanical component. Here we present the electrical component of muscle contraction. Muscle fibers, like other cells of the body, are electrically excitable. A description of the electrical properties of skeletal muscle fibers is presented next, and later sections illustrate the role of these properties in contraction. Action potentials travel from the brain or spinal cord along the axons to muscle fibers and cause them to contract. Electrically excitable cells, like other cells, are polarized. That is, the inside of most cell membranes is negatively charged compared with the outside. Thus, a voltage difference, or electrical charge difference, exists across each cell membrane. This charge difference across the cell membrane of an unstimulated cell is called the resting membrane potential (figure 7.6).

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PROCESS Figure

PROCESS Figure 7.6 APR **Measuring the Resting Membrane Potential**

A device called an oscilloscope is able to measure the resting membrane potential in skeletal muscle. The recording electrode is inside the plasma membrane, and the reference electrode is outside. Here, a potential difference of about −85 mV is recorded, with the inside of the plasma membrane negative with respect to the outside of the plasma membrane.

Apply

Would the resting membrane potential be closer to or farther from zero if the number of K^+ leak channels in the plasma membrane were increased beyond what is depicted in this figure?

Ion Channels

In order to understand the electrical properties of skeletal muscle fibers, it will help to review the permeability characteristics of cell membranes and the role that membrane transport proteins play in their permeability. The phospholipid bilayer interior is a hydrophobic environment, which inhibits the movement of charged particles, particularly ions, across the cell membrane; however, the basis

of the electrical properties of skeletal muscle cells is the movement of ions across the cell membrane. Recall from chapter 3 that ions can move across the cell membrane through ion channels. There are two major types of ion channels: (1) leak and (2) gated. These two types of channels contribute to the electrical properties of both a resting cell and a stimulated cell. In resting cells, the leak ion channels allow for the slow leak of ions down their concentration gradient. Like all membrane transport proteins, leak channels are specific for a particular ion. The gated ion channels are most important in stimulated cells. It is their presence that governs the production of action potentials.

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The Resting Membrane Potential

Electrically excitable cells are specialized to respond to electrical stimuli. At rest, these cells have an electrical charge difference across the cell membrane. In actuality, all cells in the body have this electrical charge difference, but neurons and muscle fibers contain specialized components that allow them to utilize this charge difference. In an unstimulated cell, this charge difference is called the **resting membrane potential.** Although we call it the resting membrane potential, the cell is more like a sprinter in starting blocks; it is ready to respond at a moment's notice. The resting membrane potential is the result of three factors: (1) The concentration of K^+ inside the cell membrane is higher than that outside the cell membrane, (2) the concentration of Na^+ outside the cell membrane is higher than that inside the cell membrane, and (3) the cell membrane is more permeable to K^+ than to Na^+.

Figure 7.6 illustrates the establishment of the resting membrane potential.

❶ The concentration of K^+ inside the cell membrane is higher than that outside the cell membrane. The concentration of Na^+ outside the cell membrane is higher than that inside the cell membrane. In addition, negatively charged molecules, such as proteins, are "trapped" inside the cell because the cell membrane is impermeable to them.

❷ The concentration gradient for an ion determines whether it will enter or leave the cell. Because most excitable cells have many more K^+ leak ion channels than Na^+ leak ion channels, the cell membrane is more permeable to K^+ than to Na^+. K^+ leaks out of the cell faster than Na^+ leaks into the cell. When gated Na^+ channels open, Na^+ enters the cell because Na^+ is in higher concentration outside the cell. In a similar fashion, when gated K^+ channels open, K^+ leaves the cell.

Because K^+ is positively charged, its movement from inside the cell to outside causes the inside of the cell membrane to become even more negatively charged compared with the outside. Potassium ions diffuse down their concentration gradient only until the charge difference across the cell membrane is great enough to prevent any additional diffusion of K^+ out of the cell. Therefore, the resting membrane potential is an equilibrium in which the tendency for K^+ to diffuse out of the cell is opposed by the negative charges inside the cell. These negative charges inside the cell tend to attract the positively charged K^+ back into the cell.

❸ It is the active transport of Na^+ and K^+ by the sodium-potassium pump that maintains the uneven distribution of Na^+ and K^+ across the cell membrane (see chapter 3). In a resting cell, the sodium-potassium pump transports K^+ from outside the cell to the inside and transports Na^+ from inside the cell to the outside. The details of the resting membrane potential are described more fully in chapter 8. The potential difference is reported as a negative number because the inner surface of the cell membrane is negative compared with the outside.

Apply It 1

Given that Na^+ entry is the reason nerve cells or muscle fibers become activated, describe a mechanism by which some anesthetics might "deaden" pain nerves.

Action Potentials

An action potential occurs when the excitable cell is stimulated. The action potential is a reversal of the resting membrane potential such that the inside of the cell membrane becomes positively charged compared with the outside. This charge reversal occurs because ion channels open when a cell is stimulated. The diffusion of ions through these channels changes the charge across the cell membrane and produces an action potential. An action potential lasts from approximately 1 millisecond to a few milliseconds, and it has two phases: (1) depolarization and (2) repolarization. Figure 7.7 shows the changes that occur in the membrane potential during an action potential.

❶ Before a neuron or a muscle fiber is stimulated, the gated Na^+ and K^+ ion channels are closed.

❷ When the cell is stimulated, ligand-gated Na^+ channels open and Na^+ diffuses into the cell. The positively charged Na^+ makes the inside of the cell membrane depolarized (more positive). If the depolarization causes the membrane potential to reach **threshold,** an action potential is triggered. Threshold is the membrane potential at which gated Na^+ channels open. The **depolarization phase** of the action potential is a brief period during which further depolarization occurs and the inside of the cell becomes even more positively charged.

❸ As the inside of the cell becomes positive, this voltage change causes additional permeability changes in the cell membrane, which stop depolarization and start repolarization. The **repolarization phase** is the return of the membrane potential to its resting value. It occurs when ligand-gated Na^+ channels close and gated K^+ channels open. When K^+ moves out of the cell, the inside of the cell membrane becomes more negative and the outside becomes more positive. The action potential ends, and the resting membrane potential is reestablished by the sodium-potassium pump. Next, we consider the specific communication between a motor neuron and the skeletal muscle fiber.

PROCESS Figure

PROCESS Figure 7.7 APR **Gated Ion Channels and the Action Potential**

Step 1 illustrates the status of Na^+ and K^+ channels in a resting cell. Steps 2 and 3 show how the channels open and close to produce an action potential. Next to each step, the charge difference across the cell membrane is illustrated.

Understand **Would the resting membrane potential be closer to or farther from zero if the number of K^+ leak channels in the cell membrane were increased beyond what is depicted in this figure?**

The Function of the Neuromuscular Junction

Recall that each muscle fiber is innervated by a branch of a motor neuron at the neuromuscular junction. This point of contact between the axon terminal and the sarcolemma results in an action potential in the muscle fiber. The primary stimulus for this action potential is the release of acetylcholine from the motor neuron. Figure 7.8 outlines the steps that occur at the neuromuscular junction to generate muscle contraction

❶ When an action potential reaches the presynaptic terminal of a motor neuron, it causes gated calcium ion (Ca^{2+}) channels in the cell membrane of the axon to open; as a result, Ca^{2+} diffuses into the axon terminal.

❷ Once inside the cell, the Ca^{2+} causes the contents of a few synaptic vesicles to be secreted by exocytosis from the presynaptic terminal into the synaptic cleft.

❸ The acetylcholine molecules are released from the synaptic vesicles.

❹ The acetylcholine molecules then diffuse across the cleft and bind to ligand-gated Na^+ channels in the sarcolemma causing them to open.

❺ Sodium ions then diffuse into the muscle fiber, causing depolarization. In skeletal muscle, each action potential in the motor neuron causes a depolarization in the muscle fiber that exceeds threshold. This will produce an action potential in the muscle fiber.

❻ Acetylcholine then unbinds from the gated Na^+ channels, which then close.

❼ The enzyme **acetylcholinesterase** (AS-ee-til-koh-lin-ES-ter-ase) rapidly breaks down acetylcholine in the synaptic cleft into acetic acid and choline. Acetylcholinesterase keeps acetylcholine from accumulating within the synaptic cleft, where it would act as a constant stimulus at the motor end-plate, producing continuous contraction in the muscle fiber.

❽ Motor neurons actively reabsorb choline molecules into the axon terminal. The choline molecules then combine with the acetic acid produced within the neuron to produce acetylcholine.

❾ Recycling choline molecules requires less energy and is more rapid than continuously synthesizing new acetylcholine molecules. The acetylcholine molecules are then taken up by synaptic vesicles.

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PROCESS Figure

PROCESS Figure 7.8 APR **Function of the Neuromuscular Junction**

ACh is released in response to an action potential at the neuromuscular junction.

Apply **In the autoimmune disorder myasthenia gravis, antibodies are formed against acetylcholine receptors, reducing the number of receptors in the neuromuscular junction. How would this affect skeletal muscle contraction? How would prescribing a medication that is an acetylcholinesterase inhibitor help?**

Muscle Contraction

Action potentials produced in the sarcolemma of a skeletal muscle fiber can lead to contraction of the muscle fiber. The contraction of the fiber is due to the second aspect of muscle contraction, the mechanical component. The link between the electrical and mechanical components occurs at the triad (see figure 7.2). Recall that Ca^{2+}, which is key for contraction, is stored in the sarcoplasmic reticulum. The sarcoplasmic reticulum actively transports Ca^{2+} into its lumen; thus, the concentration of Ca^{2+} is much higher within the sarcoplasmic reticulum than in the sarcoplasm of a resting muscle fiber. Muscle contraction begins with the muscle fiber at its resting membrane potential. Release of acetylcholine at the neuromuscular junction will produce an action potential in the sarcolemma (see figure 7.8).

Figure 7.9 illustrates how the events at the neuromuscular junction and the action potential along the sarcolemma result in muscle contraction.

❶ An action potential is propagated along the motor neuron.

❷ The action potential in the motor neuron stimulates the opening of voltage-gated Ca^{2+} channels.

❸ The influx of Ca^{2+} into the motor neuron causes the secretion of acetylcholine.

❹ The acetylcholine opens ligand-gated Na^{+} channels in the sarcolemma.

❺ The resulting action potential in the muscle fiber travels along the entire sarcolemma.

❻ The action potentials also move down the T tubule membranes.

❼ The T tubules wrap around sarcomeres, where actin and myosin overlap and carry action potentials into the interior of the muscle fiber. There, the action potentials cause gated Ca^{2+} channels in the terminal cisternae of the sarcoplasmic reticulum to open. When the Ca^{2+} channels open, Ca^{2+} rapidly diffuses out of the sarcoplasmic reticulum and into the sarcoplasm surrounding the myofibrils.

❽ Once in the sarcoplasm, Ca^{2+} binds to the troponin molecules of the actin myofilaments. Binding Ca^{2+} to troponin causes the tropomyosin to move, which exposes attachment sites on the actin myofilaments. The myosin heads then bind to the exposed attachment sites on actin to form cross-bridges. Muscles contract when cross-bridges move.

❾ ATP molecules are broken down into ADP and P, which releases energy needed to move the myosin heads. The heads of the myosin myofilaments bend, causing the actin to slide past the myosin. As long as Ca^{2+} is present, the cycle repeats.

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PROCESS Figure

PROCESS Figure 7.9 APR **Summary of Skeletal Muscle Contraction**

A muscle contraction starts with an action potential in a motor neuron and results in the myofilaments sliding past one another.

What will happen in a muscle fiber if threshold along the sarcolemma is not reached?

Cross-Bridge Movement

The mechanical component of muscle contraction is called **cross-bridge cycling.** This rapid sequence of events will cause the sarcomeres to shorten and the muscle will contract. The energy from one ATP molecule is required for each cross-bridge cycle. Before each cycle, the myosin head is in its resting ("high-energy") position.

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Figure 7.10 details the steps that cause shortening of the sarcomere, which leads to a contracted muscle.

❶ The myosin head stores energy from ATP breakdown that occurred during the previous cycle. The myosin head will remain in the resting position until the muscle fiber is stimulated by a motor neuron initiating the events of muscle contraction.

❷ Once the Ca^{2+} binds to the troponin and the attachment sites on the actin are exposed, the myosin heads quickly bind to them.

❸ Binding of the myosin heads to the attachment sites on the actin forms the cross-bridges and triggers a rapid movement of the myosin heads at their hinged region. The movement of the myosin head is called the **power stroke.** Because the myosin head is bound to the actin, the actin myofilament is pulled past the myosin myofilament toward the H zone of the sarcomere. Thus, the two myofilaments are "sliding" past each other. However, the myosin myofilament doesn't move, it is the actin myofilament that moves. Compare the myosin head to the wire of a traditional mouse trap. Which position of the myosin head would be equivalent to a mouse trap that has been set?

❹ Binding of ATP to the myosin head causes it to detach from the actin.

❺ The myosin head breaks down ATP into ADP and P, which remain attached to the myosin heads.

❻ The myosin heads return to their resting position. This is called the **recovery stroke,** and it returns the myosin head to its "high-energy" position from its "low-energy" position. In the "high-energy" position, the myosin myofilament can bind farther down the actin myofilament to another attachment site, and pull the actin myofilament even closer to the H zone, further shortening the sarcomere.

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PROCESS Figure

Figure 7.10 APR **Breakdown of ATP and Cross-Bridge Movement During Muscle Contraction**

Calcium ions expose myosin attachment sites for the myosin heads. Binding of the myosin heads to actin allows for sliding of the filaments. ATP breakdown resets the myosin heads.

Apply

Shortly after a person dies, Ca^{2+} diffuses out of the sarcoplasmic reticulum and the body becomes very stiff and rigid, a phenomenon called rigor mortis (RIG-er MOR-tis; stiffness + death). Given ATP's role in myosin head movement, propose an explanation for rigor mortis.

During a single contraction, each myosin myofilament undergoes the cycle of cross-bridge formation, movement, release, and return to its original position many times. Many cycles of power and recovery strokes occur during each muscle contraction. Imagine that your hands are holding onto a rope. If you pull an object closer to you using the rope, how might you accomplish this without moving your feet? Draw a diagram of your hands and the rope, and label the diagram using myofilament-specific terms. While the muscle is relaxed, energy stored in the heads of the myosin molecules is held in reserve until the next contraction. When Ca^{2+} is released from the sarcoplasmic

reticulum in response to an action potential, the cycle of cross-bridge formation, movement, and release, which results in contraction, begins again.

Muscle Relaxation

Muscle relaxation occurs when acetylcholine is no longer released at the neuromuscular junction. The lack of action potentials along the sarcolemma stops Ca^{2+} release from the sarcoplasmic reticulum and Ca^{2+} is actively transported back into the sarcoplasmic reticulum. As the Ca^{2+} concentration decreases in the sarcoplasm, the Ca^{2+} diffuses away from the troponin molecules and tropomyosin again blocks the attachment sites on the actin molecules. As a consequence, cross-bridges cannot re-form and the muscle relaxes.

Thus, energy is needed for both muscle contraction and relaxation. Three major ATP-dependent events are required for muscle relaxation:

1. After an action potential has occurred in the muscle fiber, the sodium-potassium pump must actively transport Na^+ out of the muscle fiber and K^+ into the muscle fiber to return to and maintain resting membrane potential.
2. ATP is required to detach the myosin heads from the attachment sites for the recovery stroke.
3. ATP is needed for the active transport of Ca^{2+} into the sarcoplasmic reticulum from the sarcoplasm.

Because the return of Ca^{2+} into the sarcoplasmic reticulum is much slower than the diffusion of Ca^{2+} out of the sarcoplasmic reticulum, a muscle fiber takes at least twice as long to relax as it does to contract.

7.5 WHOLE SKELETAL MUSCLE PHYSIOLOGY

Learning Outcomes *After reading this section, you should be able to*

A. Describe a muscle twitch and the events that occur in each phase of a twitch.
B. Describe a motor unit and how motor unit number affects muscle control.
C. Explain how whole muscles respond in a graded fashion and how the force of contraction can be increased.
D. Describe wave summation in terms of incomplete tetanus and complete tetanus.
E. Distinguish between isometric and isotonic contractions.
F. Relate how muscle tone is maintained.

The Muscle Twitch

The response of a muscle fiber to a single action potential along its motor neuron is called a muscle **twitch**. A single isolated twitch exists primarily under artificial conditions in a laboratory, but it can be recorded using a special apparatus. A twitch has three phases (figure 7.11). The three phases are (1) lag, (2) contraction, and (3) relaxation.

Figure 7.11 **Phases of a Muscle Twitch**
Hypothetical muscle twitch in a single muscle fiber. After the stimulus, there is a short lag phase, followed by a contraction phase and a relaxation phase.

Phases of a Twitch

The **lag phase**, or *latent phase,* is the gap between the time of stimulus application to the motor neuron and the beginning of contraction. The lag phase is the time during which the action potential is traveling along the axon, the events at the neuromuscular junction occur, and the action potential travels along the sarcolemma and releases Ca^{2+} from the sarcoplasmic reticulum. The **contraction phase** commences once the Ca^{2+} released from the sarcoplasmic reticulum initiates cross-bridge formation and cross-bridge cycling. The **relaxation phase** is much longer than the contraction phase, because the concentration of Ca^{2+} in the sarcoplasm decreases slowly due to active transport into the sarcoplasmic reticulum.

Types of Muscle Contractions

There are two major types of muscle contractions: (1) isometric contractions and (2) isotonic contractions. The type of muscle contraction differs based on whether the muscle is able to shorten when it contracts. In **isometric** (eye-soh-MET-rik) **contractions**, the muscle does not shorten. This type of contraction increases the tension in the muscle, but the length of the muscle stays the same. Isometric contractions happen if you try to lift something that is far too heavy for you. They also happen when you stand still and your postural muscles hold your spine erect. The postural muscles don't shorten because they are held in place by bones that don't move when standing still. In **isotonic** (EYE-soh-TON-ik) **contractions**, the muscle shortens. This type of contraction increases the tension in the muscle and decreases the length of the muscle. Isotonic contractions happen any time you move your limbs in order to lift an object and move it. Because an isotonic contraction results in shortening of the muscle, an isotonic twitch may change its overall characteristics depending on how much force is needed to lift the weight. For example, if the weight is increased, the lag phase may increase because it takes the muscle longer to generate enough force to lift the weight. If the weight exceeds the amount of force the muscle can generate, the contraction becomes an isometric contraction. Thus, we see that a twitch is not representative of everyday movements, which are smooth with varying rates, but this is still a helpful way to study muscle contraction.

The change in muscle contraction strength depends on two factors: (1) the amount of force in an individual muscle fiber, called **summation**, and (2) the amount of force in a whole muscle, called **recruitment**. Increasing force in a whole muscle depends on the *total number* of muscle fibers contracting. Keep in mind, *twitch* refers to the contraction of a single muscle fiber, a motor unit, or a whole muscle. Before we examine the responses of individual fibers, a definition of motor unit will be helpful.

Motor Units

A **motor unit** consists of a single motor neuron and all the muscle fibers it innervates. An action potential in the neuron of a motor unit causes contraction of all the muscle fibers in that unit. Motor units are unique and vary in both size and sensitivity to stimulus. The size of a motor unit depends on the number of the muscle fibers in that unit. A small motor unit may have as few as 10 muscle fibers, whereas a large motor unit may have several hundred muscle fibers. This variation in motor units is the reason human skeletal muscles are capable of smooth, fluid movements.

Motor units in different muscles contain different numbers of muscle fibers. Muscles performing delicate and precise movements have many small motor units. Each motor unit may contain only a small number of muscle fibers. For example, in very delicate muscles, such as those that move the eye, the number of muscle fibers per motor unit can be less than 10. On the other hand, muscles performing more powerful, but less precise, contractions have fewer, large motor units. Each of these motor units contains many muscle fibers. For example, in the large muscles of the thigh, the

number of muscle fibers per motor unit can be several hundred. Thus, having many small motor units allows for a great deal of control over a particular muscle. Conversely, having a few, large motor units allows only for coarse control over a particular muscle.

Force of Contraction in Individual Muscle Fibers

The strength of muscle contractions varies from weak to strong. In other words, muscles respond to stimuli in a **graded** fashion. Lifting a heavy weight, or lifting something repeatedly, such as when weight lifting, is possible because individual muscle fibers can generate different amounts of force. The amount of force generated in a single muscle fiber depends on the number of cross-bridges formed. Increasing the number of cross-bridges allows the muscle fiber to contract with more force. This is similar to several people lifting a heavy object instead of just one person trying to lift it. One major factor that increases the number of cross-bridges that form in a muscle fiber is the frequency of stimulation.

For a given muscle fiber, under the same cellular conditions, muscle twitches are all-or-none events when the stimulus frequency is very low, allowing for adequate rest. However, muscles stimulated at greater frequencies first display **wave summation**, followed by **incomplete tetanus**, and finally **complete tetanus** (figure 7.12). Wave summation and tetanus result because the mechanical events of muscle twitches take much longer (1 second) to complete than do the electrical events (2 msec). Thus, a muscle fiber can generate several action potentials in the time it takes to generate a single twitch. In this repeated stimulation where action potentials arrive before twitches are completed, Ca^{2+} cannot be removed from the sarcoplasm as quickly as it is released from the sarcoplasmic reticulum. The muscle fiber forms more cross-bridges, and so the muscle fiber is unable to relax between twitches. The twitches merge together more and more (incomplete tetanus, see figure 7.12, *frequency 2*) until the muscle fiber stays completely contracted with no relaxation (complete tetanus, see figure 7.12, *frequency 4*). You may find this information helpful in answering part of the Learn to Apply It question at the beginning of this chapter.

Figure 7.12 **Multiple-Wave Summation**
Stimuli 1–4 increase in frequency. For each stimulus, the arrow indicates the start of stimulation. Stimulus frequency 1 produces successive muscle twitches with complete relaxation between stimuli. Stimulus frequencies 2–3 do not allow complete relaxation between stimuli, resulting in incomplete tetanus. Stimulus frequency 4 allows no relaxation between stimuli, resulting in complete tetanus.

Contractions in Whole Muscles

Muscle Tone

There are variations in motor unit recruitment when muscles stay contracted for long periods of time. This constant tension is called **muscle tone**. Muscle tone is responsible for keeping the back and lower limbs straight, the head upright, and the abdomen flat. Muscle tone depends on a small percentage of all the motor units contracting out of phase with one another at any point in time. The

frequency of nerve impulses causes incomplete tetanus for short periods, but the contracting motor units are stimulated in such a way that the tension produced by the whole muscle remains constant.

Types of Isotonic and Isometric Contractions

Concentric (kon-SEN-trik) contractions are isotonic contractions in which tension in the muscle is great enough to overcome the opposing resistance, and the muscle shortens. Concentric contractions result in an increasing tension as the muscle shortens. Many of the movements performed by muscles, such as lifting a loaded backpack from the floor to a tabletop, require concentric contractions. **Eccentric** (ek-SEN-trik) contractions are isotonic contractions in which tension is maintained in a muscle but the opposing resistance is great enough to cause the muscle to increase in length. For example, eccentric contractions occur when a person slowly lowers a heavy weight. Eccentric contractions produce substantial force—in fact, eccentric contractions during exercise often produce greater tension than concentric contractions do. Eccentric contractions are of clinical interest because repetitive eccentric contractions, as occur in the lower limbs of people who run downhill for long distances, tend to injure muscle fibers and muscle connective tissue.

7.6 MUSCLE FIBER TYPES

Learning Outcomes *After reading this section, you should be able to*

A. Distinguish between fast-twitch and slow-twitch muscle fibers.
B. Explain the functions for which each type is best adapted.
C. Describe how training can increase the size and efficiency of both types of muscle fibers.
D. Explain how muscle metabolism causes normal body temperature.
E. Describe how muscles respond to changes from normal body temperature.

There are two major types of skeletal muscle fibers: (1) slow-twitch and (2) fast-twitch. Not all skeletal muscles have identical functional capabilities. They differ in several respects, including the composition of their muscle fibers, which may contain slightly different forms of myosin. The myosin of slow-twitch muscle fibers causes the muscle fibers to contract more slowly and to be more resistant to fatigue, whereas the myosin of fast-twitch muscle fibers causes the muscle fibers to contract quickly and to fatigue quickly (Table 7.2). The proportion of muscle fiber types differs within individual muscles.

TABLE 7.2 Characteristics of Skeletal Muscle Fiber Types

Characteristics	Slow-Twitch Oxidative (SO) (Type I)	Fast-Twitch Oxidative Glycolytic (FOG) (Type IIa)	Fast-Twitch Glycolytic (FG) (Type IIb)
Myoglobin Content	High	High	Low
Mitochondria	Many	Many	Few
Capillaries	Many	Many	Few
Metabolism	High aerobic capacity, low anaerobic capacity	Intermediate aerobic capacity, high anaerobic capacity	Low aerobic capacity, highest anaerobic capacity
Fatigue Resistance	High	Intermediate	Low
Myosin ATPase Activity	Slow	Fast	Fast
Glycogen Concentration	Low	High	High
Location Where Fibers Are Most Abundant	Generally in postural muscles and more in lower limbs than upper limbs	Generally in lower limbs	Generally in upper limbs

Characteristics	Slow-Twitch Oxidative (SO) (Type I)	Fast-Twitch Oxidative Glycolytic (FOG) (Type IIa)	Fast-Twitch Glycolytic (FG) (Type IIb)
Functions	Maintenance of posture and performance of endurance activities	Endurance activities in endurancetrained muscles	Rapid, intense movements of short duration

Slow-Twitch Muscle Fibers

Slow-twitch muscle fibers (type I) contract more slowly, have a better-developed blood supply, have more mitochondria, and are more fatigue-resistant than fast-twitch muscle fibers. Slow-twitch muscle fibers break down ATP slowly because their myosin heads have a slow form of the enzyme that breaks down ATP. The relatively slow breakdown of ATP means that cross-bridge movement occurs slowly, which causes the muscle to contract slowly. Slow-twitch muscles have a large capacity to produce ATP using O_2. This ability is enhanced by a plentiful blood supply and the presence of numerous mitochondria and is why they are called oxidative muscle fibers. Slow-twitch muscle fibers also contain large amounts of **myoglobin** (my-oh-GLOH-bin). Myoglobin binds O_2 in muscle fibers and serves as an O_2 reservoir during increased muscle activity.

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Fast-Twitch Muscle Fibers

Fast-twitch muscle fibers (type II) have myosin heads with a fast form of the enzyme that breaks down ATP, which allows their cross-bridges to release and form more rapidly than those in slow-twitch muscle fibers. Muscles containing a high percentage of fast-twitch muscle fibers have a less-well-developed blood supply than muscles containing a high percentage of slow-twitch muscle fibers. In addition, fast-twitch muscle fibers have very little myoglobin and fewer and smaller mitochondria. Fast-twitch muscle fibers have large deposits of glycogen and are well adapted to produce small amounts of ATP quickly without O_2. These muscle fibers tend to contract rapidly for a shorter time and to fatigue relatively quickly. Fast-twitch muscle fibers come in two forms: type IIa muscle fibers, and type IIb muscle fibers (Table 7.2). Type IIa muscle fibers rely on ATP production with and without O_2, whereas type IIb muscle fibers rely almost exclusively on ATP production without O_2. This information may help you answer the Learn to Apply It question at the beginning of this chapter.

Distribution of Fast-Twitch and Slow-Twitch Muscle Fibers

Many animals have muscles that are composed primarily of either fast-twitch or slow-twitch muscle fibers. Muscles that consist mainly of fast-twitch muscle fibers will appear whitish. This is because this type of muscle has a relatively poor blood supply and very little of the dark-colored myoglobin. Chicken breast is an example of a muscle that has primarily fast-twitch muscle fibers. Chickens fly only very short distances. However, muscles that consist mainly of slow-twitch muscle fibers are darker, or reddish, in color. These muscles have a well-developed blood supply and a large amount of myoglobin. Duck breast is an example of a muscle that has mainly slow-twitch muscle fibers. Ducks fly long distances when they migrate for the winter.

Human muscles exhibit no clear separation of slow-twitch and fast-twitch muscle fibers. Most human muscles have both types of muscle fibers, although the number of each varies for each muscle. The large postural muscles of the back and lower limbs contain more slow-twitch muscle fibers, whereas the muscles of the upper limbs contain more fast-twitch muscle fibers. Trained sprinters have a greater percentage of fast-twitch muscle fibers, whereas trained long-distance runners have a higher percentage of slow-twitch muscle fibers in their lower limb muscles. Athletes who perform a variety of anaerobic and aerobic exercises tend to have a more balanced mixture of fast-twitch and slow-twitch muscle fibers.

Effects of Exercise

Neither fast-twitch nor slow-twitch muscle fibers can be easily converted to muscle fibers of the other type without specialized training. Training can increase the size and capacity of both types of muscle fibers so that they perform more efficiently. Intense exercise that requires ATP production without O_2, such as weight lifting, increases muscular strength and mass and causes fast-twitch muscle fibers to enlarge more than slow-twitch muscle fibers. Conversely, exercise in which ATP is produced with O_2 increases the vascularity of muscle and causes slow-twitch muscle fibers to enlarge more. Through specific training, a person with more fast-twitch muscle fibers can run long distances, and a person with more slow-twitch muscle fibers can increase the speed at which he or she runs.

In response to exercise, a muscle increases in size, or **hypertrophies** (high-PER-troh-fees), and increases in strength and endurance. Conversely, a muscle that is not used decreases in size, or **atrophies** (AT-roh-fees). Because muscle fiber numbers do not change appreciably during most of a person's life, atrophy and hypertrophy result from changes in the size of individual muscle fibers. New nuclei are added to muscle fibers because small **satellite cells** near skeletal muscle fibers increase in number in response to exercise and then fuse with the skeletal muscle fibers. Other elements, such as blood vessels, connective tissue, and mitochondria, also increase in number. Atrophy due to lack of exercise results from a decrease in all these elements without a decrease in muscle fiber number. However, severe atrophy, as occurs in elderly people who cannot readily move their limbs, does involve an irreversible decrease in the number of muscle fibers and can lead to paralysis.

There are two reasons athletic training increases muscle strength: (1) it increases muscle size and (2) it increases in the number of motor units recruited simultaneously by the nervous system. Improved endurance in trained muscles is in part due to improved metabolism, increased circulation to the exercising muscles, increased numbers of capillaries, more efficient respiration, and a greater capacity of the heart to pump blood.

7.7 ENERGY SOURCES FOR MUSCLE CONTRACTION

Learning Outcomes *After reading this section, you should be able to*

A. Describe four sources of energy for ATP production in muscles.
B. Distinguish between oxygen deficit and excess postexercise oxygen consumption.
C. Compare the mechanisms involved in the major types of muscle fatigue.
D. Contrast physiological contracture and rigor mortis.

Skeletal muscle fibers have three major ATP-dependent proteins: (1) the myosin head, (2) the Na^+/K^+ pump, which maintains the resting membrane potential, and (3) the Ca^{2+} pump in the sarcoplasmic reticulum. You learned in section 7.4 that skeletal muscle contraction and relaxation both require ATP in order to take place. Muscle fibers store only enough ATP to contract for about 5–6 seconds. After that, muscle fibers must synthesize additional ATP very quickly, eventually producing one ATP at the same rate as one ATP is used.

Skeletal muscle fibers produce ATP through four processes:

1. Conversion of two ADP to one ATP and one adenosine monophosphate (AMP) by the enzyme **adenylate kinase**
2. Transfer of a phosphate from a molecule called **creatine** (KREE-a-teen) **phosphate** by the enzyme creatine kinase from ADP to form ATP
3. Anaerobic production of ATP during intensive short-term exercise
4. Aerobic production of ATP during most exercise and normal conditions

We will first describe the steps in each of the four ATP-producing pathways. Then we will discuss the timeframe for each pathway: (1) immediately upon contraction, (2) when muscle contraction is short-term, and (3) when the muscle contraction is continued for several hours.

Adenylate Kinase and Creatine Kinase

Muscle fibers have two enzymes that help quickly produce small amounts of ATP. The ATP produced by these enzymes is sufficient for an additional 15 seconds of contraction beyond the initial 5–6 seconds from stored ATP. These two enzymes are (1) adenylate kinase and (2) creatine kinase.

Adenylate Kinase

Adenylate kinase, or *myokinase*, transfers one phosphate from one ADP to a second ADP, resulting in one ATP and one AMP (figure 7.13*a*).

PROCESS Figure

PROCESS Figure 7.13 **Production of ATP in Skeletal Muscle**

There are four main pathways for ATP production in skeletal muscle. (*a*) Adenylate kinase quickly converts ADP to ATP. This produces only a few seconds of ATP. (*b*) Creatine kinase uses banked phosphate from creatine phosphate for immediate ATP, but is depleted within 5-6 seconds. (*c*) Anaerobic respiration is used for short-term, intense exercise and can provide up to an additional 40 seconds of ATP. (*d*) Aerobic respiration produces ATP for hours of exercise.

Understand **A marathon runner collapses after crossing the finish line and must be carried to the medical tent. Explain why the runner's muscles were unable to contract.**

Creatine Kinase

During periods of rest, muscle fibers accumulate extra ATP. This extra ATP is utilized in muscle fibers to transfer a phosphate from the ATP to a small protein synthesized by muscle fibers called **creatine.** The transfer of the phosphate creates the molecule **creatine phosphate.** This molecule acts like a "bank" for "high-energy" phosphate. When ATP levels start to drop in a contracting muscle fiber, the enzyme **creatine kinase** will transfer a phosphate from creatine phosphate to ADP, immediately producing ATP (figure 7.13*b*).

Anaerobic Respiration

Anaerobic (an-uh-ROH-bik) **respiration** does not require O_2 and involves the breakdown of glucose to produce ATP and lactate. Anaerobic respiration produces only enough ATP to power muscle contractions for 30–40 seconds. It's important to note that exercise is not usually exclusively limited to one type of ATP production, such as anaerobic respiration. Later we will discuss the blending of the four ATP production pathways under typical muscle contraction conditions. Anaerobic respiration produces far less ATP than other pathways, but can produce ATP in a matter of a few seconds. The first step of anaerobic respiration is the enzymatic pathway, called **glycolysis** (glye-KOHL-ih-sis). In glycolysis, one glucose molecule is broken down into two molecules of **pyruvate,** producing a net gain of two ATP molecules. In anaerobic respiration, the pyruvic acid is then converted to a molecule called **lactate** (figure 7.13*c*).

Historically, ATP production in skeletal muscle was thought to be clearly delineated into purely aerobic activities versus purely anaerobic activities. It was also believed that the product of anaerobic respiration was principally lactic acid, which was considered to be a harmful waste product that must be removed from the body. However, it is now widely recognized that anaerobic respiration ultimately gives rise to lactic acid's alternate chemical form, the conjugate base, lactate. Moreover, it is now known that lactate is a critical metabolic intermediate that is formed and used continuously even under fully aerobic conditions. Lactate is produced by skeletal muscle cells at all times, but particularly during exercise, and is subsequently broken down (65–70%) or used to make new glucose (30–35%). Thus, the aerobic and anaerobic mechanisms of ATP production are linked through lactate.

Aerobic Respiration

Aerobic (ai-ROH-bik) **respiration** requires O_2 and breaks down glucose to produce ATP, CO_2, and H_2O (figure 7.13*d*). The ATP from aerobic respiration supplies 95% of the total ATP required by a cell and provides enough ATP for hours of muscle contraction as long as O_2 is readily available. Aerobic respiration occurs mostly in the mitochondria and is much more efficient than anaerobic respiration. With aerobic respiration pathways, the breakdown of a single glucose molecule produces up to 36 ATP, 18 times more than anaerobic respiration. The first step in aerobic respiration is also glycolysis. However, instead of converting the two pyruvic acid molecules into lactate, as in anaerobic respiration, the two pyruvic acid molecules are transported into the mitochondria where the bulk of the ATP is produced.

ATP Production as Exercise Progresses

At the onset of exercise, the small ATP reserve in muscle fibers is quickly depleted. It is at this point that direct production of ATP by adenylate kinase and creatine kinase occurs, but this is also rapidly depleted after about 15 seconds.

When a muscle fiber is working too strenuously for ATP stores and creatine phosphate to be able to provide enough ATP, anaerobic respiration predominates. Typically, the fast-twitch muscle fibers are the primary anaerobic muscle fibers. The fast-twitch muscle fibers break down glucose into the intermediate lactate, which can be shuttled to adjacent slow-twitch muscle fibers to make ATP or to be secreted into the blood for uptake by other tissues, such as the liver, to make new glucose. Thus, in skeletal muscle, the fast-twitch muscle fiber anaerobic pathways and the slow-twitch muscle fiber aerobic pathways are not mutually exclusive. Instead, they work together, with lactate being the product of the fast-twitch muscle fiber anaerobic pathways, which then serves as the starting point of the slow-twitch muscle fiber aerobic pathways. Although aerobic respiration produces many more ATP molecules than anaerobic respiration does, the rate at which the ATP molecules are produced is slower. Resting muscles or muscles involved in long-term exercise, such as long-distance running or other endurance activities, use aerobic respiration for ATP synthesis. Aerobic respiration can provide enough ATP for hours of exercise.

Muscle Fatigue

Fatigue is a temporary state of reduced work capacity. Without fatigue, muscle fibers would be worked to the point of structural damage to them and their supportive tissues. Historically it was thought that buildup of lactic acid and the corresponding drop in pH (acidosis) was the major cause of fatigue. However, it is now established that there are multiple mechanisms underlying muscular fatigue.

These mechanisms include:

1. Acidosis and ATP depletion due to either an increased ATP consumption or a decreased ATP production
2. Oxidative stress, which is characterized by the buildup of excess reactive oxygen species (ROS; free radicals)
3. Local inflammatory reactions

Acidosis and ATP Depletion

Anaerobic respiration results in breakdown of glucose to lactate and protons, accounting for lowered pH. Lowered pH has several cellular effects, including decreased effectiveness of Ca^{2+} on actin and overall less Ca^{2+} release from the sarcoplasmic reticulum. Lactic acidosis can also result when liver dysfunction results in reduced clearance of lactate (such as using it to produce glucose, for example). Usually, increased lactate levels are due to increased anaerobic respiration production of ATP when aerobic respiration production of ATP is reduced. Increases in lactate are also seen in patients with mitochondrial disorders and chronic obstructive pulmonary disease (COPD).

However, to what extent ATP reductions are responsible for muscular fatigue is still not clear. Recent studies have demonstrated that cytoplasmic ATP levels stay relatively constant even in the face of decreasing muscle force production. But decreased ATP does cause fatigue. More specifically, it is the *localized* decreases in ATP levels or those associated with specific transport systems that are correlated with muscle fatigue.

Oxidative Stress

During intense exercise, increases in ROS production cause the breakdown of proteins, lipids, or nucleic acids. In addition, ROS trigger an immune system chemical called interleukin (IL)-6. IL-6 is a mediator of inflammation, which is the most likely cause of muscle soreness.

Inflammation

In addition to the stimulation of IL-6 by ROS, which causes inflammation, the immune system is directly activated by exercise. T lymphocytes, a type of white blood cell, migrate into heavily worked muscles. The presence of immune system intermediates increases the perception of pain, which most likely serves as a signal to protect those tissues from further damage.

An example of muscle fatigue occurs when a runner collapses on the track and must be helped off. The runner's muscle can no longer function regardless of how determined the runner is. Under conditions of extreme muscular fatigue, muscle may become incapable of either contracting or relaxing. This condition, called **physiological contracture,** occurs when there is too little ATP to bind to myosin myofilaments. Because binding of ATP to the myosin heads is necessary for cross-bridge release between the actin and myosin, the cross-bridges between the actin and myosin myofilaments cannot be broken, and the muscle cannot relax.

The most common type of fatigue, **psychological fatigue,** involves the central nervous system rather than the muscles themselves. The muscles are still capable of contracting, but the individual "perceives" that continued muscle contraction is impossible. A determined burst of activity in a tired runner in response to pressure from a competitor is an example of how psychological fatigue can be overcome.

Although fatigue reduces power output, the overall benefit is that it prevents complete exhaustion of ATP reserves, which could lead to severe damage of the muscle fibers.

Apply It 2

After a 10-mile run with a sprint at the end, a runner continues to breathe heavily for a time. Indicate the type of respiration that is producing energy during the run, during the sprint, and after the run.

Muscle Soreness

Following vigorous exercise, people sometimes experience muscle pain, which can last for several days. The pain is more common in untrained people. In addition, highly repetitive eccentric muscle contractions produce pain more readily than concentric contractions do. The pain is related to the effects of inflammatory chemicals on the muscle fibers. In people with exercise-induced muscle soreness, enzymes that are normally found inside muscle fibers can be detected in the extracellular fluid. These enzymes are able to leave the muscle fibers because injury has increased the permeability of plasma membranes, or has even ruptured them. Also found in the extracellular fluid of muscles are fragments of collagen, indicating that both muscle fibers and the connective tissue of muscles have been injured. Exercise schedules that alternate exercise with periods of rest, such as lifting weights every other day, provide time for the repair of muscle tissue.

Oxygen Deficit and Excess Postexercise Oxygen Consumption

When a person exercises, there are two distinct phases of O_2 use: (1) at the onset of exercise or increase in exercise intensity, called the oxygen deficit, and (2) after exercise has ended, called excess postexercise oxygen consumption. **Oxygen deficit** is the lag time between when a person begins to exercise and when they begin to breathe more heavily because of the exercise. **Excess postexercise oxygen consumption** is the lag time before breathing returns to its preexercise rate once exercise stops. These changes in breathing patterns reflect muscles' need for more oxygen to produce ATP through aerobic respiration.

Oxygen deficit is insufficient oxygen consumption relative to increased activity at the onset of exercise. This deficit must be repaid during and after exercise, once oxygen consumption catches up with the increased activity level. At the onset of exercise, muscles primarily acquire the ATP they need from the creatine kinase and myokinase systems, as well as from anaerobic respiration—three systems that can supply ATP relatively quickly and without requiring oxygen (see figure 7.13). The ability of aerobic respiration to supply ATP at the onset of exercise lags behind that of the creatine kinase system and anaerobic respiration. This explains the lag between the onset of exercise and the need for increased oxygen.

Excess postexercise oxygen consumption is the elevated oxygen consumption that occurs after exercise has ended. A small part of the excess postexercise oxygen is used to "repay" the oxygen deficit incurred at the onset of exercise, but most of the excess postexercise oxygen is used to support metabolic processes that restore homeostasis after it was disturbed during exercise. Such disturbances include exercise-related increases in body temperature, changes in intra- and extracellular ion concentrations, and changes in levels of metabolites and hormones. Excess postexercise oxygen consumption generally lasts minutes to hours, depending on the individual's physical conditioning and the length and intensity of the exercise session. In extreme cases, such as following a marathon, excess postexercise oxygen consumption can last as long as 15 hours.

7.8 SMOOTH MUSCLE AND CARDIAC MUSCLE

Learning Outcomes *After reading this section, you should be able to*

A. Distinguish among skeletal, smooth, and cardiac muscle.

Smooth muscle cells are small and spindle-shaped, usually with one nucleus per cell (Table 7.1). They contain less actin and myosin than do skeletal muscle cells, and the myofilaments are not organized into sarcomeres. As a result, smooth muscle cells are not striated. Smooth muscle cells contract more slowly than skeletal muscle cells when stimulated by neurotransmitters from the nervous system and do not develop an oxygen deficit. The resting membrane potential of some smooth muscle cells fluctuates between slow depolarization and repolarization phases.

Smooth muscle is under involuntary control, whereas skeletal muscle is under voluntary motor control. Certain hormones, such as those that regulate the digestive system, can stimulate smooth muscle to contract. Some smooth muscle is also **autorhythmic.** Muscle cells that are autorhythmic can spontaneously generate action potentials and then contract in some circumstances.

Smooth muscle cells are organized to form layers. Most of those cells have gap junctions, specialized cell-to-cell contacts (see chapter 4), that allow action potentials to spread to all the smooth muscle cells in a tissue. Thus, all the smooth muscle cells tend to function as a unit and contract at the same time.

Cardiac muscle shares some characteristics with both smooth and skeletal muscle (Table 7.1). Cardiac muscle cells are long, striated, and branching, with usually only one nucleus per cell. The actin and myosin myofilaments are organized into sarcomeres, but the distribution of myofilaments is not as uniform as in skeletal muscle. As a result, cardiac muscle cells are striated, but not as distinctly striated as skeletal muscle. When stimulated by neurotransmitters, the rate of cardiac muscle contraction is between those of smooth and skeletal muscle. Cardiac muscle contraction is autorhythmic. Cardiac muscle exhibits limited anaerobic respiration. Instead, it continues to contract at a level that can be sustained by aerobic respiration and consequently does not fatigue.

Cardiac muscle cells are connected to one another by specialized structures that include desmosomes and gap junctions called **intercalated** (in-TER-kah-lay-ted) **disks.** Intercalated disks allow action potentials to be conducted directly from cell to cell. Cardiac muscle cells function as a single unit. As a result, an action potential in one cardiac muscle cell can stimulate action potentials in adjacent cells, causing all to contract together. As with smooth muscle, cardiac muscle is under involuntary control and is influenced by hormones, such as epinephrine.

7.9 GENERAL PRINCIPLES OF SKELETAL MUSCLE ANATOMY

Learning Outcomes *After reading this section, you should be able to*

A. Define the following: origin, insertion, agonist, antagonist, synergist, and prime mover.
B. Give an example of each: origin, insertion, agonist, antagonist, synergist, and prime mover.

The majority of our muscles extend from one bone to another and cross at least one joint. At each end, the muscle is connected to the bone by a **tendon.** Tendons take on many forms. They can be (1) long and ropelike, (2) broad and sheetlike (called **aponeuroses;** AP-oh-nyoo-ROH-sez), or (3) very short. A **retinaculum** (ret-ih-NAK-you-lum; bracelet) is a band of connective tissue that holds down the tendons at each wrist and ankle. Muscle contraction causes most body movements by pulling one of the bones toward the other across the movable joint. However, not all muscles are attached to bone at both ends. For example, some facial muscles attach to the skin, which moves as the muscles contract, such as when smiling.

The two points of attachment of each muscle are its origin and insertion. The **origin** is the most stationary, or fixed, end of the muscle. In the case of multiple origins, each origin is called a head. The **insertion** is the end of the muscle attached to the bone undergoing the greatest movement. Origins are usually, but not always, proximal or medial to the insertion of a given muscle that is movable. The part of the muscle between the origin and the insertion is the **belly** (figure 7.14).

Figure 7.14 **Muscle Attachment**

Muscles are attached to bones by tendons. The biceps brachii has two origins that originate on the scapula. The triceps brachii has three origins that originate on the scapula and humerus. The biceps tendon inserts onto the radial tuberosity and onto nearby connective tissue. The triceps brachii inserts onto the olecranon of the ulna.

The specific body movement a muscle contraction causes is called the muscle's **action.** Muscles are typically studied in groups called **agonists** (AG-on-ists) and **antagonists** (an-TAG-oh-nists). The action of a single muscle or group of muscles (agonist) is opposed by that of another muscle or group of muscles (antagonist). For example, the biceps brachii flexes (bends) the elbow, and the triceps brachii extends the elbow. In the example of elbow flexion, the biceps brachii is the agonist (flexes), whereas the triceps brachii is the antagonist (extends). When extending the elbow, the muscles' roles are reversed; the triceps brachii is the agonist and the biceps brachii is the antagonist. Most joints in the body have agonist and antagonist groups or pairs.

Muscles also tend to function in groups to accomplish specific movements. Members of a group of muscles working together to produce a movement are called synergists (SIN-er-jist). One group of synergists includes the deltoid, biceps brachii, and pectoralis major working together to flex the shoulder. Another example of synergists is the biceps brachii and the brachialis working to flex the elbow. Among a group of synergists, if one muscle plays the major role in accomplishing the desired movement, it is called the **prime mover.** It may surprise you to know that the brachialis is the prime mover in flexing the elbow. Because the biceps brachii is easier to see when flexing the elbow, you might assume it, rather than the brachialis, is the prime mover. **Fixators** are muscles that hold one bone in place relative to the body while a usually more distal bone is moved. For example, the muscles of the scapula act as fixators to hold the scapula in place while other muscles contract to move the humerus. Furthermore, many muscles are members of more than one group, depending on the type of movement being produced. For example, the anterior part of the deltoid muscle functions with the flexors of the shoulder, whereas the posterior part functions with the extensors of the shoulder.

Muscle Names

The name of a specific muscle is based on one or more of its characteristics. The following are seven common characteristics used to name muscles: (1) location, (2) size, (3) shape, (4) orientation of fascicles, (5) origin and insertion, (6) number of heads, and (7) function (figure 7.15; Table 7.3). Recognizing the descriptive nature of muscle names makes learning those names much easier.

1. *Location.* A pectoralis (*chest*) muscle is located in the chest, a gluteus (*buttock*) muscle is in the buttock, and a brachial (*arm*) muscle is in the arm.

2. *Size.* The gluteus maximus (*large*) is the largest muscle of the buttock, and the gluteus minimus (*small*) is the smallest. A longus (*long*) muscle is longer than a brevis (*short*) muscle. In addition, a second part to the name immediately tells us there is more than one related muscle. For example, if there is a brevis muscle, most likely a longus muscle is present in the same area.
3. *Shape.* The deltoid (*triangular*) muscle is triangular in shape, a quadratus (*quadrate*) muscle is rectangular, and a teres (*round*) muscle is round.
4. *Orientation of fascicles.* A rectus (*straight, parallel*) muscle has muscle fascicles running in the same direction as the structure with which the muscle is associated, whereas the fascicles of an oblique muscle lie at an angle to the length of the structure.
5. *Origin and insertion.* The sternocleidomastoid has its origin on the sternum and clavicle and its insertion on the mastoid process of the temporal bone. The brachioradialis originates in the arm (*brachium*) and inserts onto the radius.
6. *Number of heads.* A biceps muscle has two heads (origins), and a triceps muscle has three heads (origins).
7. *Function.* Recall from chapter 6 that body movements have names, for example, abduction and adduction. Abductors and adductors are the muscles that cause that type of movement. Abduction moves a structure away from the midline, and adduction moves a structure toward the midline.

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Figure 7.15 **Body Musculature**

(a) Anterior view of the superficial skeletal muscles. *(b)* Posterior view of the superficial skeletal muscles.

TABLE 7.3 Fascicle Arrangement

Pattern of Fascicle Arrangement	Shape of Muscle	Examples
Circular Fascicles arranged in a circle around an opening; act as sphincters to close the opening		Orbicularis oris Orbicularis oculi

Pattern of Fascicle Arrangement	Shape of Muscle	Examples
Convergent Broadly distributed fascicles converge at a single tendon	 Triangular	Pectoralis major Pectoralis minor
Parallel Fascicles lie parallel to one another and to the long axis of the muscle	 Trapezium	Trapezius
	 Rhomboidal	Rhomboideus
	 Quadrate	Rectus abdominis
Pennate Fascicles originate from a tendon that runs the length of the entire muscle. Three different patterns.		

Pattern of Fascicle Arrangement	Shape of Muscle	Examples
Unipennate Fascicles on only one side of the tendon		Palmar interosseus Semimembranosus
Bipennate Fascicles on both sides of the tendon		Rectus femoris
Multipennate Fascicles arranged at many places around the central tendon. Spread out at angles to many smaller tendons.		Deltoid
Fusiform Fascicles lie parallel to long axis of muscle. Belly of muscle is larger in diameter than ends.		Biceps brachii (two-headed; shown) Triceps brachii (three-headed)

Examining surface anatomy can also be a great help in understanding muscle anatomy. We have pointed out certain muscles of the upper and lower limbs that can be seen on the surface of the body, and figure 7.15 shows the most superficial muscles. An overview of the superficial skeletal muscles appears in figure 7.15. Muscles of the head and neck, trunk, and limbs are described in the following

sections. The tables in this chapter summarize the information you need to guide your study of the muscular system. As you study, first locate the muscle on the figure, and then find its description in the corresponding table. Thinking about the muscles in terms of groups of actions and then practicing the actions on yourself will help you remember the details of each muscle. Try not to become too overwhelmed. By studying one muscle table at a time with persistence, you will soon have a better understanding of the muscles of the body.

7.10 MUSCLES OF THE HEAD AND NECK

Learning Outcomes *After reading this section, you should be able to*

A. List the major muscles involved in various facial expressions.
B. List the muscles or groups of muscles involved in mastication, tongue movement, and swallowing.

The muscles of the head and neck include those involved in forming facial expressions, chewing, moving the tongue, swallowing, producing sounds, moving the eyes, and moving the head and neck.

Facial Expression

In humans, facial expressions are important components of nonverbal communication. Several muscles act to move the skin around the eyes and eyebrows (figure 7.16 and Table 7.4). (1) The **occipitofrontalis** (ok-SIP-i-toh-fron-TAH-lis) raises the eyebrows. (2) The **orbicularis oculi**(or-BIK-you-LA-ris, circular; OK-you-lie, eye) are around the eyes. These muscles tightly close the eyelids, and cause wrinkles in the skin at the lateral corners of the eyes.

Figure 7.16 APR **Muscles of Facial Expression and Mastication**

(*a*) Lateral view of facial muscles as seen from the right side. (*b*) Drawing and photograph of the anterior view of facial muscles.

(b) McGraw Hill Education/Photo and Dissection by Christine Eckel

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TABLE 7.4 Muscles of Facial Expression (see figure 7.16)

Muscle	Origin	Insertion	Action
Buccinator (BUK-sin-AY-tor)	Maxilla and mandible	Orbicularis oris at corner of mouth	Draws corner of mouth posteriorly; compresses cheek to hold food between teeth
Depressor anguli oris (dee-PRES-or AN-gyu-lie OR-is)	Lower border of mandible	Skin of lip near corner of mouth	Lowers corner of mouth; "frown"
Levator labii superioris (le-VAY-tor LAY-bee-eye soo-PER-ee-OR-is)	Maxilla	Skin and orbicularis oris of upper lip	Raises upper lip; sneer
Occipitofrontalis (ok-SIP-i-toh-fron-TAH-lis)	Occipital bone	Skin of eyebrow and nose	Moves scalp; raises eyebrows

Muscle	Origin	Insertion	Action
Orbicularis oculi (or-BIK-you-LA-ris OK-you-lie)	Maxilla and frontal bones	Circles orbit and inserts onto skin around eyelids	Closes eyes; blinking, winking, squinting
Orbicularis oris (or-BIK-you-LA-ris OR-is)	Nasal septum, maxilla, and mandible	Fascia and other muscles of lips	Closes and purses lips; "kissing"
Zygomaticus major (ZY-goh-MAT-ih-kus)	Zygomatic bone	Angle of mouth	Elevates and abducts upper lip and corner of mouth; "smile"
Zygomaticus minor (ZY-goh-MAT-ih-kus)	Zygomatic bone	Orbicularis oris of upper lip	Elevates and abducts upper lip; "smile"

Several other muscles function in moving the lips and the skin surrounding the mouth (figure 7.16). (1) The **orbicularis oris** (OR-is; mouth) is around the mouth. (2) The **buccinator** (BUK-sin-AY-tor; *bucca,* cheek) is in the walls of the cheeks. Together these muscles are sometimes called the kissing muscles because they pucker the mouth. (1) The buccinator also flattens the cheeks as in whistling or blowing a trumpet and is therefore sometimes called the trumpeter's muscle. Smiling is accomplished primarily by the **zygomaticus** (ZY-goh-MAT-ih-kus) muscles, which elevate the upper lip and corner of the mouth. Sneering is accomplished by the **levator labii superioris** (le-VAY-tor LAY-bee-eye soo-PER-ee-OR-is) because the muscle elevates one side of the upper lip. Frowning and pouting are largely performed by the **depressor anguli oris** (dee-PRES-or AN-gyu-lie OR-is), which depresses the corner of the mouth.

Understand **Apply It 3**

Which facial muscles would be used to carry out the following nonverbal facial communications: surprise, winking, frowning, and sneering?

Mastication

The four pairs of muscles for chewing, or **mastication** (mas-tih-KAY-shun), are some of the strongest muscles in the body (Table 7.5). (1) The **temporalis** (TEM-poh-RAY-lis) and (2) **masseter** (ma-SEE-ter) muscles (figure 7.16) can be easily seen and felt on the side of the head during mastication. (3 and 4) The **pterygoid** (TER-ih-goyd) muscles, consisting of two pairs, are deep to the mandible.

TABLE 7.5 Muscles of Mastication (see figure 7.16)

Muscle	Origin	Insertion	Action
Temporalis (TEM-poh-RAY-lis)	Temporal fossa	Anterior portion of mandibular ramus and coronoid process	Elevates and draws mandible posteriorly; closes jaw
Masseter (ma-SEE-ter)	Zygomatic arch	Lateral side of mandibular ramus	Elevates and pushes mandible anteriorly; closes jaw
Lateral pterygoid (TER-ih-goyd) (not shown in illustration)	Lateral pterygoid plate and greater wing of sphenoid	Condylar process of mandible and articular disk	Pushes mandible anteriorly and depresses mandible; closes jaw
Medial pterygoid (not shown in illustration)	Lateral pterygoid plate of sphenoid and tuberosity of maxilla	Medial surface of mandible	Pushes mandible anteriorly and elevates mandible; closes jaw

Tongue and Swallowing Muscles

The tongue is very important in mastication and speech. It moves food around in the mouth and, with the buccinator muscle, holds the food in place while the teeth grind the food. The tongue pushes food up to the palate and back toward the pharynx to initiate swallowing. The tongue consists of a mass of (1) **intrinsic muscles,** which are located entirely within the tongue and change its shape. (2) The **extrinsic muscles** are located outside the tongue but are attached to and move the tongue (figure 7.17 and Table 7.6).

Figure 7.17 **Tongue and Swallowing Muscles**
Muscles of the tongue, hyoid, pharynx, and larynx as seen from the right.

TABLE 7.6 Tongue and Swallowing Muscles (see figure 7.17)

Muscle	Origin	Insertion	Action
Tongue muscles			
Intrinsic (not shown) Extrinsic	Inside tongue Bones around oral cavity or soft palate	Inside tongue Onto tongue	Changes shape of tongue Moves tongue
Hyoid muscles			
Suprahyoid (e.g., geniohyoid, stylohyoid, and hyoglossus)	Base of skull, mandible	Hyoid bone	Elevates or stabilizes hyoid
Infrahyoid (e.g., thyrohyoid)	Sternum, larynx	Hyoid bone	Depresses or stabilizes hyoid
Soft palate muscles (not shown)	Skull or soft palate	Palate, tongue, or pharynx	Moves soft palate, tongue, or pharynx
Pharyngeal muscles			
Elevators (not shown) Constrictors Superior (not shown) Middle Inferior	Soft palate and auditory tube Larynx and hyoid	Pharynx Pharynx	Elevate pharynx Constrict pharynx

Swallowing involves a number of structures and their associated muscles, including (1) the hyoid muscles, (2) soft palate, (3) pharynx (throat), and (4) larynx (voicebox). The **hyoid** (HYE-oyd) **muscles** are divided into a suprahyoid group (superior to the hyoid bone) and an infrahyoid group (inferior to the hyoid bone) (figure 7.17 and Table 7.6). When the suprahyoid muscles hold the hyoid

bone in place from above, the infrahyoid muscles can elevate the larynx. To observe this effect, place your hand on your larynx (Adam's apple) and swallow.

The muscles of the soft palate and pharynx close the posterior opening to the nasal cavity during swallowing, preventing food and liquid from entering the nasal cavity. When we swallow, muscles elevate the pharynx and larynx and then constrict the pharynx. Specifically, (1) the **pharyngeal** (fa-RIN-jee-al) **elevators** elevate the pharynx, and (2) the **pharyngeal constrictors** constrict the pharynx from superior to inferior, forcing the food into the esophagus. Pharyngeal muscles also open the auditory tube, which connects the middle ear to the pharynx. Opening the auditory tube equalizes the pressure between the middle ear and the atmosphere. This is why it is sometimes helpful to chew gum or swallow when ascending or descending a mountain in a car or changing altitude in an airplane.

Neck Muscles

The deep neck muscles (figure 7.18 and Table 7.7) include (1) neck flexors and (2) neck extensors. Neck flexors originate on the anterior surface of the vertebral bodies. Neck extensors originate on the posterior surface of the vertebral bodies. Lateral and posterior neck muscles rotate and laterally flex the head. The prime mover of the lateral muscle group, the **sternocleidomastoid** (STER-noh-kly-doh-MAS-toid) muscle (see figure 7.16*a*), is easily seen on the anterior and lateral sides of the neck. Contraction of only one sternocleidomastoid muscle rotates the head. Contraction of both sternocleidomastoids can either flex or extend the head and neck.

Figure 7.18 APR **Deep Neck and Back Muscles**

The upper limb, pectoral girdle, and associated muscles have been removed. On the right, the erector spinae muscles are shown. On the left, these muscles are removed to reveal the deeper back muscles.

TABLE 7.7 Neck Muscles (see figures 7.15, 7.16, and 7.22)

Muscle	Origin	Insertion	Action
Deep neck muscles			
Flexors (not shown)	Anterior side of vertebrae	Base of skull	Flex head and neck
Extensors	Posterior side of vertebrae	Base of skull	Extend head and neck
Sternocleidomastoid (STER-noh-kly-doh-MAS-toid)	Manubrium of sternum and medial part of clavicle	Mastoid process and nuchal line of skull	Individually rotate head; together flex neck
Trapezius (tra-PEE-zee-us)	Posterior surface of skull and upper vertebral column (C7–T12)	Clavicle, acromion process, and scapular spine	Extends and laterally flexes neck

Understand **Apply It 4**

Shortening of the right sternocleidomastoid muscle rotates the head in which direction?

7.11 TRUNK MUSCLES

Learning Outcome *After reading this section, you should be able to*

A. Describe the muscles of the trunk and the actions they produce.

Trunk muscles include those that move (1) the vertebral column, (2) the thorax, (3) the abdominal wall, and (4) the pelvic diaphragm and perineum.

Vertebral Column Muscles

In humans, maintenance of erect posture is due to very strong back muscles. The **erector spinae** (ee-REK-tor SPEE-nee) group of muscles on each side of the back are primarily responsible for keeping the back straight and the body erect (Table 7.8 and figure 7.18). **Deep back muscles,** located between the spinous and transverse processes of adjacent vertebrae, are responsible for several movements of the vertebral column, including extension, lateral flexion, and rotation. When the deep back muscles are stretched abnormally or torn, muscle strains and sprains of lumbar vertebral ligaments can occur, resulting in low back pain. Treatments include anti-inflammatory medication and RICE (*r*est, *i*ce, *c*ompression, and *e*levation). Low back exercises can also help the problem.

TABLE 7.8 Muscles Acting on the Vertebral Column (see figure 7.18)

Muscle	Origin	Insertion	Action
Superficial			
Erector spinae (ee-REK-tor SPEE-nee) divides into three columns:	Sacrum, ilium, vertebrae, and ribs	Ribs, vertebrae, and skull	Extends vertebral column; maintains posture
Iliocostalis (IL-ee-oh-kos-TAH-lis)			
Longissimus (lon-GIS-i-mus)			
Spinalis (spy-NAY-lis)			
Deep back muscles	Vertebrae	Vertebrae	Extend vertebral column and help bend vertebral column laterally

Thoracic Muscles

The muscles of the thorax (figure 7.19 and Table 7.9) are involved almost entirely in the process of breathing. The **external intercostals** (IN-ter-KOS-tulz; between ribs) elevate the ribs during inspiration. The **internal intercostals** depress the ribs during forced expiration. However, the major movement produced in the thorax during quiet breathing is accomplished by the dome-shaped **diaphragm** (DIE-ah-fram). When it contracts, the dome is flattened, causing the volume of the thoracic cavity to increase, resulting in inspiration.

Figure 7.19 APR **Muscles of the Thorax**
(*a*) Anterior view shows a few selected intercostal muscles and the diaphragm. (*b*) Lateral view shows the external and internal intercostals.

TABLE 7.9 Muscles of the Thorax (see figures 7.19 and 7.22)

Muscle	Origin	Insertion	Action
Scalenes (SKAY-leens)	Cervical vertebrae	First and second ribs	Inspiration; elevate ribs
External intercostals (IN-ter-KOS-tulz)	Inferior edge of each rib	Superior edge of next rib below origin	Inspiration; elevate ribs
Internal intercostals (IN-ter-KOS-tulz)	Superior edge of each rib	Inferior edge of next rib above origin	Forced expiration; depress ribs
Diaphragm (DIE-ah-fram)	Inferior ribs, sternum, and lumbar vertebrae	Central tendon of diaphragm	Inspiration; depress floor of thorax

Abdominal Wall Muscles

The anterior abdominal body wall muscles (figure 7.20 and Table 7.10) flex and rotate the vertebral column, compress the abdominal cavity, and hold in and protect the abdominal organs. In a relatively muscular person with little fat, a vertical indentation, extending from the sternum through the navel to the pubis, is visible. This tendinous area of the abdominal wall, called the **linea alba** (LIN-ee-ah AL-bah; white line), consists of white connective tissue rather than muscle. On each side of the linea alba is the **rectus abdominis** (REK-tus ab-DOM-i-nis; *rectus,* straight) muscle. **Tendinous intersections** cross the rectus abdominis at three or more locations, causing the abdominal wall of a lean, well-muscled person to appear segmented. Lateral to the rectus abdominis

are three layers of muscle. From superficial to deep, these muscles are (1) the **external abdominal oblique,** (2) the **internal abdominal oblique,** and (3) the **transversus abdominis** (trans-VER-sus ab-DOM-in-is) muscles. The fasciculi of these three muscle layers are oriented in different directions. When these muscles contract, they flex and rotate the vertebral column or compress the abdominal contents.

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Figure 7.20 APR **Muscles of the Anterior Abdominal Wall**

(*a*) In this anterior view, windows reveal the various muscle layers. (*b*) A cross-sectional view of the muscle layers.

TABLE 7.10 Muscles of the Abdominal Wall (see figures 7.15, 7.20, 7.22)

Muscle	Origin	Insertion	Action
Rectus abdominis (REK-tus ab-DOM-i-nis)	Pubic crest and pubic symphysis	Xiphoid process and inferior ribs	Flexes vertebral column; compresses abdomen
External abdominal oblique	Ribs 5–12	Iliac crest, inguinal ligament, and fascia of rectus abdominis	Compresses abdomen; flexes and rotates vertebral column
Internal abdominal oblique	Iliac crest, inguinal ligament, and lumbar fascia	Ribs 10–12 and fascia of rectus abdominis	Compresses abdomen; flexes and rotates vertebral column
Transversus abdominis (trans-VER-sus ab-DOM-in-is)	Costal cartilages 7–12, lumbar fascia, iliac crest, and inguinal ligament	Xiphoid process, fascia of rectus abdominis, and pubic tubercle	Compresses abdomen

Pelvic Diaphragm and Perineal Muscles

The pelvis is a ring of bone (see chapter 6) with an inferior opening that is closed by a muscular floor, through which the anus and the urogenital openings penetrate (Table 7.11). The pelvic floor is called the **pelvic diaphragm.** It consists of (1) the **coccygeus** (kok-SIH-jee-us) muscle and (2) the **levator ani** (AN-eye) muscle. Just inferior to (beneath) the pelvic diaphragm is a diamond-shaped area called the **perineum** (PER-ih-NEE-um; figure 7.21). The anterior half of the perineum is the **urogenital triangle,** and the posterior half of the perineum is the **anal triangle** (see chapter 19). During pregnancy, the muscles of the pelvic diaphragm and urogenital triangle may be stretched by the extra weight of the fetus, and specific exercises are designed to strengthen them.

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TABLE 7.11 Muscles of the Pelvic Diaphragm and Perineum (see figure 7.21)				
Muscle	**Origin**	**Insertion**	**Nerve**	**Action**
Pelvic Diaphragm				
Coccygeus (kok-SIH-jee-us)	Ischial spine	Coccyx	S3 and S4	Forms pelvic floor; supports pelvic organs
Levator ani (lee-VAY-tor, le-VAY-ter AN-eye)	Posterior pubis and ischial spine	Sacrum and coccyx	Fourth sacral	Elevates anus; supports pelvic organs
Perineum Urogenital triangle				
Bulbospongiosus (BUL-boh-spun-jee-OH-ses)	Male—central tendon of perineum and median raphe of penis	Dorsal surface of penis and bulb of penis	Pudendal	Compresses base of penis; ejects urine or semen; erects penis
	Female—central tendon of perineum	Base of clitoris	Pudendal	Erects clitoris
Ischiocavernosus (ISH-ee-oh-KAV-er-noh-ses)	Ischial ramus	Corpus cavernosum	Perineal	Compresses base of penis or clitoris
External urethral sphincter (you-ree-thral SFINK-ter; not illustrated)	Pubic ramus	Median raphe	Pudendal	Constricts urethra to stop urine flow
Transverse perineal muscle (PAIR-ih-NEE-al)				
Deep	Ischial ramus	Median raphe	Pudendal	Supports pelvic floor
Superficial	Ischial ramus	Central perineal	Pudendal	Fixes central tendon
Anal triangle				
External anal sphincter (AY-nal SFINK-ter)	Coccyx	Central tendon of perineum	Fourth sacral and pudendal	Keeps orifice of anal canal closed; relaxes during defecation

Figure 7.21 **Muscles of the Pelvic Diaphragm and Perineum**
(*a*) Inferior view of the pelvic diaphragm muscles in the male. (*b*) Inferior view of the pelvic diaphragm muscles in the female.

7.12 UPPER LIMB MUSCLES

Learning Outcome *After reading this section, you should be able to*

A. List the muscle groups involved in the movements of the arm, forearm, and hand.

The muscles of the upper limb include those that attach the limb and pectoral girdle to the body and those in the arm, forearm, and hand.

Scapular Movements

The upper limb is primarily connected to the body by muscles: (1) the **trapezius** (tra-PEE-zee-us), (2) the **levator scapulae** (le-VAY-tor SKAP-you-lee), (3) the **rhomboids** (ROM-boidz), (4) the **serratus** (ser-AH-tus; serrated) **anterior,** and (5) the **pectoralis** (PEK-toh-RA-lis) **minor** all are important muscles for scapular attachment and movement (figure 7.22 and Table 7.12). These muscles act as fixators to hold the scapula firmly in position when the muscles of the arm contract. The scapular muscles also move the scapula into different positions, thereby increasing the range of movement of the upper limb. The trapezius forms the upper line from each shoulder to the neck. The origin of the serratus anterior from the first eight or nine ribs can be seen along the lateral thorax.

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Figure 7.22 APR **Muscles of the Shoulder**

(*a*) Posterior view of the neck and upper shoulder. The left side shows the superficial muscles. On the right, the superficial muscles are removed to show the deep muscles. (*b*) Posterior view of the thoracic region, with the trapezius and deltoid muscles removed. (*c*) Anterior view of the thoracic region.

TABLE 7.12 Muscles Acting on the Scapula (see figures 7.15, 7.22, and 7.23)

Muscle	Origin	Insertion	Action
Levator scapulae (le-VAY-tor SKAP-you-lee)	Transverse processes of C1–C4	Superior angle of scapula	Elevates, retracts, and rotates scapula; laterally flexes neck
Pectoralis minor (PEK-toh-RA-lis)	Ribs 3–5	Coracoid process of scapula	Depresses scapula or elevates ribs
Rhomboids (ROM-boidz)			
Major	Spinous processes of T1–T4	Medial border of scapula	Retracts, rotates, and fixes scapula
Minor	Spinous processes of T1–T4	Medial border of scapula	Retracts, slightly elevates, rotates, and fixes scapula

Muscle	Origin	Insertion	Action
Serratus anterior (ser-AH-tus)	Ribs 1–9	Medial border of scapula	Rotates and protracts scapula; elevates ribs
Trapezius (tra-PEE-zee-us)	Posterior surface of skull and spinous processes of C7–T12	Clavicle, acromion process, and scapular spine	Elevates, depresses, retracts, rotates, and fixes scapula; extends neck

Arm Movements

The (1) **pectoralis major** and (2) **latissimus dorsi** (lah-TIS-i-mus DOR-sigh) muscles (figure 7.23*a* and Table 7.13; see figure 7.22*c*) attach the arm to the thorax. The pectoralis major adducts the arm and flexes the shoulder. It can also extend the shoulder from a flexed position. The latissimus dorsi medially rotates and adducts the arm and powerfully extends the shoulder. Because a swimmer uses these three motions during the freestyle stroke, the latissimus dorsi is often called the swimmer's muscle.

Figure 7.23 APR **Arm Muscles**

(*a*) Drawing and photograph of chest and arm muscles, anterior view. (*b*) Lateral view of arm muscle as seen from the right side.

(a) McGraw Hill Education/Photo and Dissection by Christine Eckel

TABLE 7.13 Arm Movements (see figures 7.15, 7.22, 7.23, and 7.24)

Muscle	Origin	Insertion	Action
Deltoid (DEL-toyd)	Clavicle, acromion process, and scapular spine of scapula	Deltoid tuberosity of humerus	Flexes and extends shoulder; abducts and medially and laterally rotates arm
Latissimus dorsi (lah-TIS-i-mus DOR-see)	Spinous processes of T7–L5, sacrum and iliac crest, and inferior angle of scapula in some people	Medial crest of intertubercular groove of humerus	Extends shoulder; adducts and medially rotates arm

Muscle	Origin	Insertion	Action
Pectoralis major (PEK-toh-RA-lis)	Clavicle, sternum, superior six costal cartilages, and abdominal muscles	Lateral crest of intertubercular groove of humerus	Flexes shoulder; extends shoulder from flexed position; adducts and medially rotates arm
Teres major (TER-ees)	Lateral border of scapula	Medial crest of intertubercular groove of humerus	Extends shoulder; adducts and medially rotates arm
Rotator Cuff			
Infraspinatus (IN-frah-spih-NAH-tus)	Infraspinous fossa of scapula	Greater tubercle of humerus	Stabilizes and extends shoulder and laterally rotates arm
Subscapularis (SUB-skap-you-LAR-is)	Subscapular fossa of scapula	Lesser tubercle of humerus	Stabilizes and extends shoulder and medially rotates arm
Supraspinatus (SOO-prah-spi-NAH-tus)	Supraspinous fossa of scapula	Greater tubercle of humerus	Stabilizes shoulder and abducts arm
Teres minor (TER-ees)	Lateral border of scapula	Greater tubercle of humerus	Stabilizes and extends shoulder; adducts and laterally rotates arm

The **rotator cuff muscles** stabilize the shoulder joint by holding the head of the humerus in the glenoid cavity during arm movements, especially abduction. These muscles form a cuff or cap over the proximal humerus (Table 7.13; see figure 7.22*b,c*). A rotator cuff injury involves damage to one or more of these muscles or their tendons. The **deltoid** (DEL-toyd) muscle attaches the humerus to the scapula and clavicle and is the major abductor of the upper limb (figure 7.23). The pectoralis major forms the upper chest, and the deltoid forms the rounded mass of the shoulder (see figure 7.23). The deltoid is a common site for administering injections.

Forearm Movements

The arm can be divided into anterior and posterior compartments. The **triceps brachii** (TRY-seps BRAH-kee-eye; three heads, arm), the primary extensor of the elbow, occupies the posterior compartment (figure 7.23*b* and Table 7.14). The anterior compartment is occupied mostly by (1) the **biceps** (BY-seps) **brachii** and (2) the **brachialis** (BRAH-kee-AL-is), the primary flexors of the elbow. The **brachioradialis** (BRAH-kee-oh-RAY-dee-AL-is), which is actually a posterior forearm muscle, helps flex the elbow.

TABLE 7.14 Arm Muscles (see figures 7.15, 7.22, 7.23, and 7.24)

Muscle	Origin	Insertion	Action
Biceps brachii (BY-seps BRAH-kee-eye)	Long head—supraglenoid tubercle of scapula Short head—coracoid process of scapula	Radial tuberosity and aponeurosis of biceps brachii	Flexes elbow; supinates forearm; flexes shoulder
Brachialis (BRAH-kee-AL-is)	Anterior surface of humerus	Coronoid process of ulna	Flexes elbow

Muscle	Origin	Insertion	Action
Triceps brachii (TRY-seps BRAH-kee-eye)	Long head—lateral border of scapula Lateral head—lateral and posterior surface of humerus Medial head—posterior humerus	Olecranon process of ulna	Extends elbow; extends shoulder; adducts arm

Supination and Pronation

Supination of the forearm, or turning the flexed forearm so that the palm is up, is accomplished by the **supinator** (SOO-pi-nay-ter) (figure 7.24 and Table 7.15) and the biceps brachii, which tends to supinate the forearm while flexing the elbow. Pronation, turning the forearm so that the palm is down, is a function of two **pronator** (proh-NAY-ter) muscles.

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Figure 7.24 APR **Muscles of the Forearm**
(*a*) Anterior view. The flexor retinaculum has been removed. (*b*) Posterior view.

TABLE 7.15 Forearm Muscles (see figure 7.24)

Muscle	Origin	Insertion	Action
Anterior Forearm			
Palmaris longus (pawl-MAR-is LON-gus)	Medial epicondyle of humerus	Aponeurosis over palm	Tightens skin of palm
Flexor carpi radialis (KAR-pee RAY-dee-a-lis)	Medial epicondyle of humerus	Second and third metacarpal bones	Flexes and abducts wrist
Flexor carpi ulnaris (KAR-pee ul-NAR-is)	Medial epicondyle of humerus and ulna	Pisiform	Flexes and adducts wrist
Flexor digitorum profundus (DIJ-ih-TOR-um proh-FUN-dus) (not shown)	Ulna	Distal phalanges of digits 2–5	Flexes fingers and wrist
Flexor digitorum superficialis (SOO-per-FISH-ee-AY-lis)	Medial epicondyle of humerus, coronoid process, and radius	Middle phalanges of digits 2–5	Flexes fingers and wrist
Pronator			

Muscle	Origin	Insertion	Action
Quadratus (proh-NAY-ter kwah-drah-tus)	Distal ulna	Distal radius	Pronates forearm
Teres (proh-NAY-ter TE-rees)	Medial epicondyle of humerus and coronoid process of ulna	Radius	Pronates forearm
Posterior Forearm			
Brachioradialis (BRAH-kee-oh-RAY-dee-A-lis)	Lateral supracondylar ridge of humerus	Styloid process of radius	Flexes elbow
Extensor carpi radialis brevis (KAR-pee RAY-dee-a-lis BREV-is) (not shown)	Lateral epicondyle of humerus	Base of third metacarpal bone	Extends and abducts wrist
Extensor carpi radialis longus (LON-gus)	Lateral supracondylar ridge of humerus	Base of second metacarpal bone	Extends and abducts wrist
Extensor carpi ulnaris (KAR-pee ul-NAR-is)	Lateral epicondyle of humerus and ulna	Base of fifth metacarpal bone	Extends and adducts wrist
Extensor digitorum (DIJ-ih-TOR-um)	Lateral epicondyle of humerus	Extensor tendon expansion over phalanges of digits 2–5	Extends fingers and wrist
Supinator (SOO-pi-nay-ter)	Lateral epicondyle of humerus and ulna	Radius	Supinates forearm (and hand)

Wrist and Finger Movements

The twenty muscles of the forearm can also be divided into anterior and posterior groups. Only a few of these muscles, the most superficial, appear in Table 7.15 and figure 7.24. Most of the anterior forearm muscles are responsible for flexion of the wrist and fingers, whereas most of the posterior forearm muscles cause extension. A strong band of fibrous connective tissue, the retinaculum (figure 7.24*b*), covers the flexor and extensor tendons and holds them in place around the wrist so that they do not "bowstring" (pull away from the bone) during muscle contraction. Because the retinaculum does not stretch as a result of pressure, this characteristic is a contributing factor in carpal tunnel syndrome.

The **flexor carpi** (KAR-pie) muscles flex the wrist, and the **extensor carpi** muscles extend the wrist. The tendon of the flexor carpi radialis serves as a landmark for locating the radial pulse (figure 7.24*a*). The tendons of the wrist extensors are visible on the posterior surface of the forearm (figure 7.24*b*). Forceful, repeated contraction of the wrist extensor muscles, as occurs in a tennis backhand, may result in inflammation and pain where the extensor muscles attach to the lateral humeral epicondyle. This condition is sometimes referred to as "tennis elbow." Flexion of the fingers is the function of the **flexor digitorum** (DIJ-ih-TOR-um; flexor of the digits, or fingers). Extension of the fingers is accomplished by the **extensor digitorum.** The tendons of this muscle are very visible on the dorsal surface of the hand (figure 7.24*b*). The thumb has its own set of flexors, extensors, adductors, and abductors. The little finger has some similar muscles.

Nineteen muscles, called **intrinsic hand muscles,** are located within the hand. **Interossei** (IN-ter-OS-ee-eye; between bones) muscles, located between the metacarpal bones, are responsible for abduction and adduction of the fingers. Other intrinsic hand muscles are involved in the many possible movements of the thumb and fingers. These muscles account for the fleshy masses at the base of the thumb and little finger and the fleshy region between the metacarpal bones of the thumb and index finger.

7.13 LOWER LIMB MUSCLES

Learning Outcomes *After reading this section, you should be able to*

A. List the muscle groups involved in the movements of the thigh, leg, and foot.

The muscles of the lower limb include those located in (1) the hip, (2) the thigh, (3) the leg, and (4) the foot.

Thigh Movements

Several hip muscles originate on the hip bone and insert onto the femur (figure 7.25 and Table 7.16). The anterior muscle, the **iliopsoas** (IL-ee-oh-SOH-us), flexes the hip (figure 7.25*a*). The posterior and lateral hip muscles consist of the **gluteal muscles** and the tensor fasciae latae. The **tensor fasciae latae** (TEN-sor FA-she-eh LAH-tee) is so named because it tenses a thick band of fascia on the lateral side of the thigh called the iliotibial tract. By so doing, it helps steady the femur on the tibia when a person is standing. The **gluteus** (GLOO-tee-us; buttock) **maximus,** which extends the hip and abducts and laterally rotates the thigh, contributes most of the mass that can be seen as the buttocks. The **gluteus medius,** which abducts and medially rotates the thigh, creates a smaller mass just superior and lateral to the maximus (see figure 7.25*b*). The gluteus maximus functions optimally to extend the hip when the thigh is flexed at a 45-degree angle. The gluteus medius is a common site for injections in the buttocks because the sciatic nerve lies deep to the gluteus maximus and could be damaged during an injection.

Figure 7.25 APR **Muscles of the Hip and Thigh**

(*a*) Anterior view. The vastus intermedius is labeled to allow for a complete listing of the quadriceps femoris muscles, but the muscle lies deep to the rectus femoris and cannot be seen in the figure. (*b*) Posterior view of the hip muscles. (*c*) Posterior view of the thigh muscles.

TABLE 7.16 Muscles Moving the Thigh (see figure 7.25)

Muscle	Origin	Insertion	Action
Iliopsoas (IL-ee-oh-SOH-us)	Iliac fossa and vertebrae T12–L5	Lesser trochanter of femur and hip capsule	Flexes hip
Gluteus maximus (GLOO-tee-us MAK-si-mus)	Posterior surface of ilium, sacrum, and coccyx	Gluteal tuberosity of femur and iliotibial tract	Extends hip; abducts and laterally rotates thigh
Gluteus medius (GLOO-tee-us MEE-dee-us)	Posterior surface of ilium	Greater trochanter of femur	Abducts and medially rotates thigh
Gluteus minimus (GLOO-tee-us MIN-i-mus) (not shown)	Posterior surface of ilium	Greater trochanter of femur	Abducts and medially rotates thigh

Muscle	Origin	Insertion	Action
Tensor fasciae latae (TEN-sor FA-she-eh LAH-tee)	Anterior superior iliac spine	Through lateral fascia of thigh to lateral condyle of tibia	Steadies femur on tibia through iliotibial tract when standing; flexes hip; medially rotates and abducts thigh

In addition to the hip muscles, some of the thigh muscles also attach to the hip bone and can move the thigh. There are three groups of thigh muscles: the anterior thigh muscles, which flex the hip; the posterior thigh muscles, which extend the hip; and the medial thigh muscles, which adduct the thigh.

Apply It 5

Consider a sprinter's stance and a bicyclist's racing posture, and explain why these athletes use these postures.

Leg Movements

The anterior thigh muscles are (1) the **quadriceps femoris** (KWAH-dri-seps fe-MOR-is; four muscles) and (2) the **sartorius** (sar-TOR-ee-us) (Table 7.17; figures 7.25). The quadriceps femoris muscles are the primary extensors of the knee. They have a common insertion, the patellar tendon, on and around the patella. The patellar ligament is an extension of the patellar tendon onto the tibial tuberosity. The patellar ligament is tapped with a rubber hammer when testing the knee-jerk reflex in a physical examination (see chapter 8). Health professionals often use one of the quadriceps muscles, the vastus lateralis, as an intermuscular injection site. The sartorius, the longest muscle in the body, is called the "tailor's muscle" because it flexes the hip and knee and rotates the thigh laterally for sitting cross-legged, as tailors used to sit while sewing.

TABLE 7.17 Leg Movements (see figures 7.15, 7.25, and 7.26)

Muscle	Origin	Insertion	Action
Anterior Compartment			
Quadriceps femoris (KWAH-dri-seps fe-MOR-is)			
Rectus femoris (REK-tus fem-oh-ris)	Ilium	Tibial tuberosity via patellar ligament	Extends knee; flexes hip
Vastus lateralis (VAS-tus lat-er-AH-lis)	Greater trochanter and linea aspera of femur	Tibial tuberosity via patellar ligament	Extends knee
Vastus medialis (VAS-tus MEE-dee-AH-lis)	Linea aspera of femur	Tibial tuberosity via patellar ligament	Extends knee
Vastus intermedius (VAS-tus IN-ter-MEE-dee-us)	Body of femur	Tibial tuberosity via patellar ligament	Extends knee
Sartorius (sar-TOR-ee-us)	Anterior superior iliac spine	Medial side of tibial tuberosity	Flexes hip and knee; laterally rotates thigh
Medial Compartment			
Adductor longus (AD-duk-ter LON-gus)	Pubis	Linea aspera of femur	Adducts and laterally rotates thigh; flexes hip
Adductor magnus (AH-duk-ter MAG-nus)	Pubis and ischium	Femur	Adducts and laterally rotates thigh; extends knee
Gracilis (GRAS-i-lis)	Pubis near symphysis	Tibia	Adducts thigh; flexes knee

Muscle	Origin	Insertion	Action
Posterior Compartment (Hamstring Muscles)			
Biceps femoris (BY-seps fem-oh-ris)	Long head—ischial tuberosity	Head of fibula	Flexes knee; laterally rotates leg; extends hip
	Short head—femur		
Semimembranosus (SE-mee-MEM-brah-NOH-sus)	Ischial tuberosity	Medial condyle of tibia and collateral ligament	Flexes knee; medially rotates leg; extends hip
Semitendinosus (SE-mee-TEN-di-NOH-sus)	Ischial tuberosity	Tibia	Flexes knee; medially rotates leg; extends hip

The posterior thigh muscles are called **hamstring muscles,** and they are responsible for flexing the knee (Table 7.17; see figures 7.15*b* and 7.25*c*). Their tendons are easily felt and seen on the medial and lateral posterior aspect of a slightly bent knee (figure 7.25*b*). The hamstrings are so named because these tendons in hogs or pigs could be used to suspend hams during curing. Animals such as wolves often bring down their prey by biting through the hamstrings, thus preventing the prey animal from running. "To hamstring" someone is therefore to render him or her helpless. A "pulled hamstring" results from tearing one or more of these muscles or their tendons, usually where the tendons attach to the hip bone.

The medial thigh muscles, the **adductor** (ad-DUK-ter, -tor) **muscles,** are primarily involved, as the name implies, in adducting the thigh (Table 7.17).

Ankle and Toe Movements

The thirteen muscles in the leg, with tendons extending into the foot, can be divided into three groups: anterior, posterior, and lateral. As with the forearm, only the most superficial muscles are illustrated in figure 7.26 and listed in Table 7.18. The anterior muscles (figure 7.26*a*) are extensor muscles involved in dorsiflexion (extension) of the foot and extension of the toes.

Figure 7.26 APR **Superficial Muscles of the Leg**
(*a–c*) Anterior, posterior, and lateral views.

TABLE 7.18	Muscles of the Leg Acting on the Leg, Ankle, and Foot (see figures 7.15, 7.25, and 7.26)		
Muscle	**Origin**	**Insertion**	**Action**
Anterior Compartment			
Extensor digitorum longus (DIJ-ih-TOR-um LON-gus)	Lateral condyle of tibia and fibula	Four tendons to phalanges of four lateral toes	Extends four lateral toes; dorsiflexes and everts foot
Extensor hallucis longus (HAL-i-sis LON-gus)	Middle fibula and interosseous membrane	Distal phalanx of great toe	Extends great toe; dorsiflexes and inverts foot

Muscle	Origin	Insertion	Action
Tibialis anterior (TIB-ee-ah-lis)	Tibia and interosseous membrane	Medial cuneiform and first metatarsal bone	Dorsiflexes and inverts foot
Fibularis tertius (peroneus tertius) (PER-oh-nee-us TER-shee-us)	Fibula and interosseous membrane	Fifth metatarsal bone	Dorsiflexes and everts foot
Posterior Compartment			
Superficial			
Gastrocnemius (GAS-trok-NEE-mee-us)	Medial and lateral condyles of femur	Through calcaneal (Achilles) tendon to calcaneus	Plantar flexes foot; flexes leg
Soleus (SOH-lee-us)	Fibula and tibia	Through calcaneal tendon to calcaneus	Plantar flexes foot
Deep			
Flexor digitorum longus (DIJ-ih-TOR-um LON-gus) (not shown)	Tibia	Four tendons to distal phalanges of four lateral toes	Flexes four lateral toes; plantar flexes and inverts foot
Flexor hallucis longus (HAL-i-sis LON-gus) (not shown)	Fibula	Distal phalanx of great toe	Flexes great toe; plantar flexes and inverts foot
Tibialis posterior (TIB-ee-ah-lis) (not shown)	Tibia, interosseous membrane, and fibula	Navicular, cuneiforms, cuboid, and second through fourth metatarsal bones	Plantar flexes and inverts foot
Lateral Compartment			
Fibularis brevis (peroneus brevis) (fib-YOU-LAH-ris BREV-is)	Fibula	Fifth metatarsal bone	Everts and plantar flexes foot
Fibularis longus (peroneus longus) (fib-YOU-LAH-ris LON-gus)	Fibula	Medial cuneiform and first metatarsal bone	Everts and plantar flexes foot

The superficial muscles of the posterior compartment of the leg (figure 7.26*b*), the **gastrocnemius** (GAS-trok-NEE-mee-us) and the **soleus** (SOH-lee-us), form the bulge of the calf (posterior leg; figure 7.26*b*). They join to form the common **calcaneal** (kal-KAY-nee-uhl; heel) **tendon,** or *Achilles tendon*. These muscles are flexors and are involved in plantar flexion of the foot. The deep muscles of the posterior compartment plantar flex and invert the foot and flex the toes.

The lateral muscles of the leg, called the **fibularis** (fib-YOU-LAH-ris) **muscles** (*peroneus*) (figure 7.26*c*), are primarily everters (turning the lateral side of the foot outward) of the foot, but they also aid in plantar flexion during locomotion.

The **intrinsic foot muscles** include twenty muscles located within the foot. These muscles all work to move the toes. These toe movements include flexion, extension, abduction, and adduction. They are arranged in a manner similar to the intrinsic muscles of the hand.

EFFECTS OF AGING ON THE SKELETAL

SYSTEM AND JOINTS

Aging skeletal muscle undergoes several changes: reduction in muscle mass, slower response time for muscle contraction, reduction in stamina, and increased recovery time. Loss of muscle fibers begins as early as 25 years of age, and by age 80 the muscle mass has been reduced by approximately 50%. Most of the loss of strength and speed is due to the loss of muscle fibers, particularly fast-twitch muscle fibers. The surface area of the neuromuscular junction decreases, and as a result, action potentials in neurons stimulate action potentials in muscle cells more slowly; thus, fewer action potentials are produced in muscle fibers. There is also a decrease in the density of capillaries in skeletal muscles so that a longer recovery period is required after exercise.

SYSTEMS PATHOLOGY

Duchenne Muscular Dystrophy

Background Information

A couple became concerned about their 3-year-old son, Greger, when they noticed that he was much weaker than other boys his age and his muscles appeared poorly developed. Greger was diagnosed with **Duchenne muscular dystrophy (DMD).** This disease involves many body systems (see figure 7.27) and is usually identified in children around 3 years of age when their parents notice slow motor development with progressive weakness and muscle wasting (atrophy). With DMD, muscular weakness begins in the pelvic girdle, causing a waddling gait. Rising from the floor by "climbing up" the legs with the hands is characteristic of patients suffering from DMD and is caused by weakness of the lumbar and gluteal muscles (figure 7.28). Within 3 to 5 years, the muscles of the shoulder girdle become involved. The replacement of muscle with connective tissue contributes to muscular atrophy and shortened, inflexible muscles called contractures. The contractures limit movements and can cause severe deformities of the skeleton. By 10 to 12 years of age, people with DMD are usually unable to walk, and few live beyond age 20. There is no effective treatment to prevent the progressive deterioration of muscles in DMD. Therapy primarily involves exercises to help strengthen muscles and prevent contractures.

Figure 7.27 Interactions Among Organ Systems and Duchenne Muscular Dystrophy
Many body systems are involved in DMD, as this diagram illustrates.

Figure 7.28 DMD Muscle Weakness
DMD is characterized by progressive muscle weakness. Rising from the floor to a standing position becomes difficult, and the patient often has to use his or her arms to push against the thighs while rising.
©Andrew J. Kornberg

Duchenne muscular dystrophy results from an abnormal gene on the X chromosome and is therefore a sex-linked (X-linked) condition. The gene is carried by females, but DMD affects males almost exclusively, at a frequency of 1 in 3000. The DMD gene is responsible for producing a protein called **dystrophin,** which plays a role in attaching myofibrils to other proteins in the cell membrane and regulating their activity. In a normal individual, dystrophin is thought to protect muscle cells against mechanical stress. In DMD patients, part of the gene is missing, and the protein it produces is nonfunctional, resulting in progressive muscular weakness and muscle contractures. Table 7.19 lists examples of other muscular system disorders.

TABLE 7.19 REPRESENTATIVE DISEASES AND DISORDERS: Muscular System

Condition	Description
Cramps	Painful, spastic contractions of a muscle; usually due to a buildup of lactic acid
Fibromyalgia (FIE-broh-my-AL-jee-uh)	Non-life-threatening, chronic, widespread pain in muscles with no known cure; also known as chronic muscle pain syndrome

Condition	Description
Hypertrophy	Enlargement of a muscle due to an increased number of myofibrils, as occurs with increased muscle use
Atrophy	Decrease in muscle size due to a decreased number of myofilaments; can occur due to disuse of a muscle, as in paralysis
Muscular dystrophy	Group of genetic disorders in which all types of muscle degenerate and atrophy
Duchenne muscular dystrophy	See Systems Pathology in this chapter
Myotonic muscular dystrophy	Muscles are weak and fail to relax following forceful contractions; affects the hands most severely; dominant trait in 1/20,000 births
Tendinitis (ten-di-NY-tis)	Inflammation of a tendon or its attachment point, due to overuse of the muscle

Apply It 6

A boy with advanced Duchenne muscular dystrophy developed pulmonary edema (accumulation of fluid in the lungs) and pneumonia caused by a bacterial infection. His physician diagnosed the condition in the following way: The pulmonary edema was the result of heart failure, and the increased fluid in the lungs provided a site where bacteria could invade and grow. The fact that the boy could not breathe deeply or cough effectively made the condition worse. How would the muscle tissues in a boy with advanced DMD with heart failure and ineffective respiratory movements differ from the muscle tissues in a boy with less advanced DMD?

SUMMARY

7.1 Functions of the Muscular System

Muscles are responsible for movement of the arms, legs, heart, and other parts of the body; maintenance of posture; respiration; production of body heat; communication; constriction of organs and vessels; and heartbeat.

1. The three types of muscle are skeletal, smooth, and cardiac.
2. Skeletal muscle is responsible for most body movements; smooth muscle is found in the walls of hollow organs and tubes and moves substances through them; and cardiac muscle is in the heart and pumps blood.

7.2 General Properties of Muscle Tissue

1. Muscle exhibits contractility (shortens forcefully), excitability (responds to stimuli), extensibility (can be stretched and still contract), and elasticity (recoils to resting length).
2. Muscle tissue shortens forcefully but lengthens passively.

7.3 Skeletal Muscle Anatomy

Skeletal muscle fibers are associated with connective tissue, blood vessels, and nerves.

Whole Skeletal Muscle Anatomy

1. Muscle fascicles, bundles of muscle fibers, are covered by the connective tissue layer called the perimysium.
2. The entire muscle is surrounded by a connective tissue layer called the epimysium.
3. Motor neurons extend together with arteries and veins through the connective tissue of skeletal muscles.
4. At the level of the perimysium, axons of motor neurons branch, and each branch projects to a muscle fiber to form a neuromuscular junction.

Skeletal Muscle Fiber Anatomy

1. A muscle fiber is a single cell consisting of a plasma membrane (sarcolemma), cytoplasm (sarcoplasm), several nuclei, and myofibrils.
2. The electrical components of a muscle fiber include the sarcolemma, the T tubules, and the sarcoplasmic reticulum.
3. The mechanical components of a muscle fiber include the myofibrils and the myofilaments.
4. Myofibrils are composed of two major protein fibers: actin and myosin.
   - Actin myofilaments consist of actin (composed of G actin monomers), tropomyosin, and troponin.
   - Myosin molecules, consisting of heads and a rodlike portion, constitute myosin myofilaments.
   - A cross-bridge forms when the myosin binds to the actin.
5. Actin and myosin are organized to form sarcomeres.
   - Sarcomeres are bound by Z disks that hold actin myofilaments.
   - Myofibrils appear striated because of A bands and I bands.
6. The neuromuscular junction is the location where a motor neuron is in close proximity to the muscle fiber. The motor neuron axon terminal contains synaptic vesicles that house the neurotransmitter, acetylcholine.
7. When muscle fibers contract, the actin and myosin filaments slide past each other, shortening the sarcomeres.

7.4 Skeletal Muscle Fiber Physiology

Excitability of Muscle Fibers

1. Plasma membranes are polarized, which means that a charge difference, called the resting membrane potential, exists across the plasma membrane.
2. The plasma membrane becomes polarized because the tendency for K^+ to diffuse out of the cell is resisted by the negative charges of ions and molecules inside the cell.
3. Ion channels are responsible for membrane permeability and the resting membrane potential.
4. Ion channels are responsible for producing action potentials.

Action Potentials

1. The charge difference across the plasma membrane of cells is the resting membrane potential.
2. Depolarization results from an increase in the permeability of the plasma membrane to Na^+.
3. The depolarization phase of the action potential results when many Na^+ channels open in an all-or-none fashion.
4. The repolarization phase of the action potential occurs when the Na^+ channels close and the K^+ channels open briefly.
5. A synaptic cleft separates the presynaptic terminal of the axon from the motor end-plate of the muscle fiber.

6. Acetylcholine released from the presynaptic terminal binds to receptors of the motor end-plate, thereby changing membrane permeability and producing an action potential.
7. After an action potential occurs, acetylcholinesterase splits acetylcholine into acetic acid and choline. Choline is reabsorbed into the presynaptic terminal to re-form acetylcholine.

Muscle Contraction

1. Invaginations of the sarcolemma form T tubules, which wrap around the sarcomeres.
2. A triad is a T tubule and two terminal cisternae (an enlarged area of sarcoplasmic reticulum).
3. Action potentials move into the T tubule system, causing Ca^{2+} channels to open and release Ca^{2+} from the sarcoplasmic reticulum.
4. Calcium ions diffuse from the sarcoplasmic reticulum to the myofilaments and bind to troponin, causing tropomyosin to move and expose active sites on actin to myosin.
5. Contraction occurs when myosin heads bind to active sites on actin, myosin changes shape, and actin is pulled past the myosin.
6. Relaxation occurs when calcium is taken up by the sarcoplasmic reticulum, ATP binds to myosin, and tropomyosin moves back so that active sites on actin are no longer exposed to myosin.

Cross-Bridge Movement

1. ATP is required for the cycle of cross-bridge formation, movement, and release.
2. ATP is also required to transport Ca^{2+} into the sarcoplasmic reticulum and to maintain normal concentration gradients across the plasma membrane.

Muscle Relaxation

1. Calcium ions are transported into the sarcoplasmic reticulum.
2. Calcium ions diffuse away from troponin, preventing further cross-bridge formation.

7.5 Whole Skeletal Muscle Physiology

The Muscle Twitch

1. A muscle twitch is the contraction of a single muscle fiber or a whole muscle in response to a stimulus.
2. A muscle twitch has lag, contraction, and relaxation phases.

Force of Contraction in Individual Muscle Fibers

1. A stimulus of increasing magnitude results in graded contractions of increased force through either summation or recruitment.
2. Incomplete tetanus is partial relaxation between contractions; complete tetanus is no relaxation between contractions.
3. A stimulus of increasing frequency increases the force of contraction (wave summation).

Contractions in Whole Muscles

1. Concentric contractions cause muscles to shorten and tension to increase.
2. Eccentric contractions cause muscle to lengthen and tension to decrease gradually.
3. Muscle tone is the maintenance of steady tension for long periods.

7.6 Muscle Fiber Types

Slow-Twitch Muscle Fibers

Slow-twitch muscle fibers break down ATP slowly and have a well-developed blood supply, many mitochondria, and myoglobin.

Fast-Twitch Muscle Fibers

Fast-twitch muscle fibers break down ATP rapidly.

1. Type IIa muscle fibers have a well-developed blood supply, more mitochondria, and more myoglobin.
2. Type IIb muscle fibers have large amounts of glycogen, a poor blood supply, fewer mitochondria, and little myoglobin.

Distribution of Fast-Twitch and Slow-Twitch Muscle Fibers

People who are good sprinters have a greater percentage of fast-twitch muscle fibers in their leg muscles, and people who are good long-distance runners have a higher percentage of slow-twitch muscle fibers.

Effects of Exercise

1. Muscles increase (hypertrophy) or decrease (atrophy) in size because of a change in the size of muscle fibers.
2. Anaerobic exercise develops type IIb muscle fibers. Aerobic exercise develops type I muscle fibers and changes type IIb muscle fibers into type IIa fast-twitch muscle fibers.

7.7 Energy Sources for Muscle Contraction

Energy for muscle contraction comes from ATP.

Adenylate Kinase and Creatine Kinase

1. Two ADP are converted by adenylate kinase to one ATP and one AMP during intense exercise.
2. ATP synthesized when ADP reacts with creatine phosphate provides energy for a short time during intense exercise.

Anaerobic Respiration

The ATP synthesized by anaerobic respiration provides energy for a short time during intense exercise. Anaerobic respiration produces ATP less efficiently but more rapidly than aerobic respiration. Lactate levels increase because of anaerobic respiration.

Aerobic Respiration

The ATP synthesized by aerobic respiration produces energy for muscle contractions under resting conditions or during exercises such as long-distance running. Although ATP is produced more efficiently, it is produced more slowly.

ATP Production as Exercise Progresses

Aerobic respiration produces more ATP than anaerobic respiration, but at a slower rate.

Muscle Fatigue

1. Fatigue, the decreased ability to do work, can be caused by the central nervous system, depletion of ATP in muscles, or depletion of acetylcholine in the neuromuscular junction.

2. Physiological contracture (the inability of muscles to contract or relax) and rigor mortis (stiff muscles after death) result from inadequate amounts of ATP.

Muscle Soreness

Soreness is caused by inflammation in the muscle.

Oxygen Deficit and Excess Postexercise Oxygen Consumption

After anaerobic respiration, aerobic respiration is higher than normal, as the imbalances of homeostasis that occurred during exercise become rectified.

7.8 Smooth Muscle and Cardiac Muscle

1. Smooth muscle cells are spindle-shaped with a single nucleus. They have actin myofilaments and myosin myofilaments but are not striated.
2. The sarcoplasmic reticulum is poorly developed, and caveolae may function as a T tubule system.
3. Cardiac muscle fibers are striated, have a single nucleus, are connected by intercalated disks (and thus function as a single unit), and are capable of autorhythmicity.

7.9 General Principles of Skeletal Muscle Anatomy

Body movements result from the contraction of skeletal muscles.

1. The less movable end of a muscle attachment is the origin; the more movable end is the insertion.
2. An agonist causes a certain movement, and an antagonist acts in opposition to the agonist.
3. Synergists are muscles that function together to produce movement.
4. Prime movers are mainly responsible for a movement. Fixators stabilize the action of prime movers.

Muscle Names

Muscles are named according to their location, size, shape, orientation of fascicles, origin and insertion, number of heads, or function.

The study of muscle anatomy is usually broken down into body regions: head and neck, trunk, upper limbs, and lower limbs.

7.10 Muscles of the Head and Neck

Facial Expression

The origins of facial muscles are on skull bones or fascia; the insertions are into the skin, causing movement of the facial skin, lips, and eyelids.

Mastication

Three pairs of muscles close the jaw; gravity opens the jaw. Forced opening is caused by the lateral pterygoids and the hyoid muscles.

Tongue and Swallowing Muscles

1. Intrinsic tongue muscles change the shape of the tongue; extrinsic tongue muscles move the tongue.
2. Hyoid muscles can depress the jaw and assist in swallowing.
3. Muscles open and close the openings to the nasal cavity, auditory tubes, and larynx.

Neck Muscles

The origins of these muscles are mainly on the cervical vertebrae (except for the sternocleidomastoid); the insertions are on the occipital bone or mastoid process. They cause

flexion, extension, rotation, and lateral flexion of the head and neck.

7.11 Trunk Muscles

Vertebral Column Muscles

1. These muscles extend, laterally flex, rotate, or flex the vertebral column.
2. A more superficial group of muscles runs from the pelvis to the skull, extending from the vertebrae to the ribs.
3. A deep group of muscles connects adjacent vertebrae.

Thoracic Muscles

1. Most respiratory movement is caused by the diaphragm.
2. Muscles attached to the ribs aid in respiration.

Abdominal Wall Muscles

Abdominal wall muscles hold and protect abdominal organs and cause flexion, rotation, and lateral flexion of the vertebral column.

Pelvic Diaphragm and Perineum Muscles

These muscles support the abdominal organs inferiorly.

7.12 Upper Limb Muscles

Scapular Movements

Six muscles attach the scapula to the trunk and enable the scapula to function as an anchor point for the muscles and bones of the arm.

Arm Movements

Seven muscles attach the humerus to the scapula. Two additional muscles attach the humerus to the trunk. These muscles cause flexion and extension of the shoulder and abduction, adduction, rotation, and circumduction of the arm.

Forearm Movements

1. Flexion and extension of the elbow are accomplished by three muscles in the arm and two in the forearm.
2. Supination and pronation are accomplished primarily by forearm muscles.

Supination and Pronation

Supination and pronation are accomplished primarily by forearm muscles.

Wrist and Finger Movements

1. Forearm muscles that originate on the medial epicondyle are responsible for flexion of the wrist and fingers. Muscles extending the wrist and fingers originate on the lateral epicondyle.
2. Extrinsic hand muscles are in the forearm. Intrinsic hand muscles are in the hand.

7.13 Lower Limb Muscles

Thigh Movements

1. Anterior pelvic muscles cause flexion of the hip.
2. Muscles of the buttocks are responsible for extension of the hip and abduction and rotation of the thigh.

Leg Movements

1. Some muscles of the thigh also act on the leg. The anterior thigh muscles extend the leg, and the posterior thigh muscles flex the leg.
2. The thigh can be divided into three compartments.
   - The anterior compartment muscles flex the hip and extend the knee.
   - The medial compartment muscles adduct the thigh.
   - The posterior compartment muscles extend the hip and flex the knee.

Ankle and Toe Movements

1. The leg is divided into three compartments.
   - Muscles in the anterior compartment cause dorsiflexion, inversion, or eversion of the foot and extension of the toes.
   - Muscles of the lateral compartment plantar flex and evert the foot.
   - Muscles of the posterior compartment flex the leg, plantar flex and invert the foot, and flex the toes.
2. Intrinsic foot muscles flex or extend, and abduct or adduct, the toes.

REMEMBERING AND UNDERSTANDING

1. List the seven major functions of the muscular system.
2. Define contractility, excitability, extensibility, and elasticity.
3. List the connective tissue layers associated with muscles.
4. What are fasciculi?
5. What is a muscle fiber?
6. Explain the relevance of the structural relationship among sarcomeres, T tubules, and the sarcoplasmic reticulum.
7. What is a sarcomere?
8. Describe the composition of a myofibril. Describe the structure of actin and myosin myofilaments.
9. Explain the resting membrane potential and how it is produced.
10. Describe the production of an action potential.
11. What is a neuromuscular junction? What happens there?
12. Describe the sliding filament model of muscle contraction.
13. Explain how an action potential results in muscle contraction.
14. Define muscle twitch, tetanus, and recruitment.
15. Describe the two ways energy is produced in skeletal muscle.
16. Explain fatigue.
17. Compare isometric, isotonic, concentric, and eccentric contraction.
18. What is muscle tone?

19. Compare slow-twitch and fast-twitch muscle fibers.
20. How do smooth muscles and cardiac muscles differ from skeletal muscles?
21. Define origin, insertion, agonist, antagonist, synergist, prime mover, and fixator.
22. Describe the muscles of facial expression.
23. What is mastication? What muscles are involved?
24. What are the intrinsic and extrinsic tongue muscles?
25. What muscles are involved in swallowing?
26. What muscles are involved in respiration?
27. Describe the functions of the muscles of the anterior abdominal wall.
28. What is primarily responsible for attaching the upper limb to the body?
29. Describe, by muscle groups, movements of the arm, forearm, and hand.
30. Describe, by muscle groups, movements of the thigh, leg, and foot.

CRITICAL THINKING

1. Harrison was frantically texting his friend before he had to store his phone for class. Before he could finish what he was typing, his hands became very tired. For a short time, he could not relax his hands to pick up his pencil. Explain what happened.
2. A researcher was investigating the fast-twitch versus slow-twitch composition of muscle tissue in the gastrocnemius muscle (in the calf of the leg) of athletes. Describe the general differences this researcher would see when comparing the muscles from athletes who were outstanding in the following events: 100-m dash, weight lifting, and 10,000-m run.
3. Describe an exercise routine that would buildup each of the following groups of muscles: anterior arm, posterior arm, anterior forearm, anterior thigh, posterior leg, and abdomen.
4. Sherri started a 100-m dash but fell to the ground in pain. Examination of her right lower limb revealed the following symptoms: The knee was held in a slightly flexed position, but she could not flex it voluntarily; she could extend the knee with difficulty, but this caused her considerable pain; and there was considerable pain and bulging of the muscles in the posterior thigh. Explain the nature of her injury.
5. Javier has a number of prize apple trees in his backyard. To prevent them from becoming infested with insects, he sprayed them with an organophosphate insecticide. Being in a rush to spray the trees before leaving town on vacation, he failed to pay attention to the safety precautions on the packaging, and sprayed the trees without using any skin or respiratory protection. Soon he experienced severe stomach cramps, double vision, difficulty breathing, and spastic contractions of his skeletal muscles. Javier's wife took him to the emergency room, where he was diagnosed with organophosphate poisoning and given medication. Soon many of Javier's symptoms subsided.
   Organophosphate insecticides exert their effects by binding to the enzyme acetylcholinesterase within synaptic clefts, rendering it ineffective. Thus, the organophosphate poison and acetylcholine "compete" for the acetylcholinesterase and, as the organophosphate poison increases in concentration, the enzyme cannot effectively degrade acetylcholine. Organophosphate poisons will prolong acetylcholine actions at both skeletal and smooth muscle synapses. These include muscles needed for movement, breathing, and gastrointestinal contractions.

Using the knowledge you gained about skeletal muscle contraction and figures 7.8 and 7.9, answer the following questions:
Explain the spastic contractions that occurred in Javier's skeletal muscles.

Answers to this chapter's odd-numbered Critical Thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

8

Nervous System

The nervous system is a communication system. At its most basic level, nervous communication occurs through electrical signals (arrow) that spread over the cell membrane of neurons and cause changes at the synapse, the communication junction between the neuron and its neighboring cell.

LEARN TO APPLY IT

Johnny found an old jar of green beans in the pantry. "These must be some that Grandma Ima canned years ago," he thought. He noticed that the lid of the jar bowed a bit. He opened the jar and the beans inside looked and smelled okay, so he prepared them for dinner. The next day, Johnny was not feeling well. His throat was dry, and he started experiencing double vision. Soon he was having difficulty breathing. He called 911. When the paramedics arrived 20 minutes later, Johnny was not breathing. He was put on a respirator and rushed to the hospital, where physicians diagnosed botulism. Johnny's recovery would be slow, and he would have to remain on a respirator. Botulism is caused by a toxin of the bacterium *Clostridium botulinum*, which grows in anaerobic (without oxygen) environments, such as improperly processed canned food. The toxin blocks the release of acetylcholine, a neurotransmitter, from neurons.

After reading about neuron communication in this chapter, explain why Johnny experienced respiratory failure as a result of the botulism.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 7 Nervous System

8.1 FUNCTIONS OF THE NERVOUS SYSTEM

Learning Outcome ***After reading this section, you should be able to***

A. List the functions of the nervous system.

The nervous system is involved in some way in nearly every body function. We can consider the nervous system as a communication system, receiving signals from and sending commands to different areas of the body. By way of this communication, the nervous system helps to coordinate the body functions to maintain homeostasis. Some major functions of the nervous system are

1. *Receiving sensory input*. Sensory receptors monitor numerous external and internal stimuli. We are aware of sensations from some stimuli, such as vision, hearing, taste, smell, touch, pain, body position, and temperature. Other stimuli, such as blood pH, blood gases, and blood pressure, are processed at a subconscious level.
2. *Integrating information*. The brain and spinal cord are the major organs for processing sensory input and initiating responses. The input may produce an immediate response, be stored as memory, or be ignored.
3. *Controlling muscles and glands*. Skeletal muscles normally contract only when stimulated by the nervous system. Thus, by controlling skeletal muscle, the nervous system controls the major movements of the body. The nervous system also participates in controlling cardiac muscle, smooth muscle, and many glands.
4. *Maintaining homeostasis*. The nervous system plays an important role in maintaining homeostasis. This function depends on the nervous system's ability to detect, interpret, and respond to changes in internal and external conditions. In response, the nervous system can stimulate or inhibit the activities of other systems to help maintain a constant internal environment.
5. *Establishing and maintaining mental activity*. The brain is the center of mental activity, including consciousness, memory, and thinking.

8.2 DIVISIONS OF THE NERVOUS SYSTEM

Learning Outcome *After reading this section, you should be able to*

A. List the divisions of the nervous system, and describe the characteristics of each.

The nervous system can be divided into two major divisions: (1) the central nervous system and the (2) peripheral nervous system (figure 8.1). The **central nervous system (CNS)** consists of the brain and spinal cord. The **peripheral nervous system (PNS)** consists of all the nervous tissue outside the CNS, including nerves and ganglia.

Figure 8.1 APR **Nervous System**
The central nervous system (CNS) consists of the brain and spinal cord. The peripheral nervous system (PNS) consists of nerves and ganglia.

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The PNS is the communication link between the CNS and the various parts of the body. The PNS carries information about the different tissues of the body to the CNS and delivers commands from the CNS to other body tissues that alter body activities. Considering this two-directional flow of information, the PNS can be subdivided into two parts:

1. The **sensory division,** or *afferent* (toward) *division*, of the PNS conducts action potentials from sensory receptors to the CNS (figure 8.2). The neurons that

transmit action potentials from the periphery to the CNS are called **sensory neurons.**

2. The **motor division,** or *efferent* (away) *division,* of the PNS conducts action potentials from the CNS to effector organs, such as muscles and glands. The neurons that transmit action potentials from the CNS toward the periphery are called **motor neurons.**

Figure 8.2 **Organization of the Nervous System**

The sensory division of the peripheral nervous system detects stimuli and conducts action potentials to the central nervous system (CNS). The CNS interprets incoming action potentials and initiates action potentials that are conducted through the motor division to produce a response. The motor division is divided into the *somatic nervous system* and the *autonomic nervous system*.

The effectors controlled by the motor division include muscle tissue and glands. Recall from chapters 4 and 7 that muscle tissue includes skeletal muscle, which is voluntarily controlled, and cardiac and smooth muscle, which are involuntarily controlled. Glands are also involuntarily controlled. The motor division can be further subdivided into two components, based on the type of effector being innervated: (1) somatic nervous system and (2) autonomic nervous system. The **somatic** (soh-MAT-ik; bodily) **nervous system** transmits action potentials from the CNS to skeletal muscles, and the **autonomic** (awe-toh-NOM-ik; self-governing) **nervous system (ANS)** transmits action potentials from the CNS to cardiac muscle, smooth muscle, and glands. The autonomic nervous system, in turn, is divided into sympathetic and parasympathetic divisions (see figure 8.2).

The **enteric nervous system (ENS)** is a unique part of the peripheral nervous system. The ENS has both sensory and motor neurons contained wholly within the digestive tract. The ENS can function without input from

the CNS or other parts of the PNS, although it is normally integrated with the CNS by sensory neurons and ANS motor neurons.

8.3 CELLS OF THE NERVOUS SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Describe the structure of neurons and the function of their components.
B. Describe the location, structure, and general function of glial cells.
C. Define and describe the structure of a nucleus, a ganglion, a nerve tract, and a nerve.

The two types of cells that make up the nervous system are (1) neurons and (2) glial cells.

Neurons

Neurons (NYUR-ons; nerve), or *nerve cells* (figure 8.3), receive stimuli, conduct action potentials, and transmit signals to other neurons or effector organs. A neuron has three parts: (1) a cell body and two types of processes, called (2) dendrites and (3) axons.

Figure 8.3 APR **Typical Neuron**

Structural features of a typical motor neuron in the PNS include a cell body and two types of cell processes: dendrites and an axon.

Each neuron **cell body** contains a single nucleus. As with any other cell, the nucleus of the neuron is the source of information for gene expression. Extensive rough endoplasmic reticulum (rough ER), a Golgi apparatus, and mitochondria surround the nucleus. Large numbers of neurofilaments (intermediate filaments) and microtubules organize the cytoplasm into distinct areas.

Dendrites (DEN-drights; trees) are short, often highly branching cytoplasmic extensions that are tapered from their bases at the neuron cell body to their tips. Most dendrites are extensions of the neuron cell body, but dendrite-like structures also project from the peripheral ends of some sensory axons. Dendrites usually receive information from other neurons or from sensory receptors and transmit the information toward the neuron cell body.

Each neuron has an **axon**, a single long cell process extending from the neuron cell body. The area where the axon leaves the neuron cell body is called the **axon hillock.** Each axon has a uniform diameter and may vary in length from a few millimeters to more than a meter. Axons of sensory neurons conduct action potentials towards the CNS, and axons of motor neurons conduct action potentials away from the CNS. Axons also conduct action potentials from one part of the brain or spinal cord to another part. An axon may remain unbranched or may branch to form **collateral** (ko-LAT-er-uhl) **axons.** Axons can be surrounded by a highly specialized insulating layer of cells called the myelin sheath (described in more detail in "Myelin Sheaths," later in this chapter).

Types of Neurons

The body's neurons vary in function and in structure. As such, neurons can be classified on the basis of their function as well as their structure. For example, referring to a neuron as a "sensory neuron" indicates that it is carrying information to the CNS from a specific receptor in the body. Alternatively, referring to a neuron as a "motor neuron" indicates that it is sending information to an effector of the body from the CNS. However, neurons are also distinguished from one another on the basis of their structure. In the structural classification, three categories of neurons exist, based on the arrangement of their processes (figure 8.4 and table 8.1).

Figure 8.4 **Types of Neurons**

Neurons are classified structurally based on the arrangement of their processes (axon and dendrites).

Table 8.1	Cells of the Nervous System (see figures 8.4 and 8.5)	
Cell Type	**Description**	**Function**
Neuron		
Multipolar	Many dendrites and one axon	Most motor neurons and most CNS neurons
Bipolar	One dendrite and one axon	Found in special sense organs, such as eye and nose
Pseudo-unipolar	Appears to have a single axon	Most sensory neurons
Glial Cells of the CNS		
Astrocytes	Highly branched	Provide structural support; regulate neuronal signaling; contributeto blood-brain barrier; help with neural tissue repair
Ependymal cells	Epithelial-like	Line ventricles of brain and central canal of the spinal cord, circulate cerebrospinal fluid (CSF); some form choroid plexuses, which produce CSF
Microglia	Small, mobile cells	Protect CNS from infection; become phagocytic in response to inflammation

Cell Type	Description	Function
Oligodendrocytes	Cells with processes that can surround several axons	Cell processes form myelin sheaths around axons or enclose unmyelinated axons in the CNS
Glial Cells of PNS		
Schwann cells	Single cells surrounding axons	Form myelin sheaths around axons or enclose unmyelinated axons in the PNS
Satellite cells	Single cells surrounding cell bodies	Support neurons, providing nutrients; protect neurons from heavy-metal poisons

1. **Multipolar neurons** have many dendrites and a single axon. Most of the neurons within the CNS and nearly all motor neurons are multipolar.
2. **Bipolar neurons** have two processes: one dendrite and one axon. Bipolar neurons are located in some sensory organs, such as in the retina of the eye and in the nasal cavity.
3. **Pseudo-unipolar neurons** have a single process extending from the cell body. This process divides into two extensions a short distance from the cell body. One extends to the periphery, and the other extends to the CNS. The two extensions function as a single axon with small, dendrite-like sensory receptors at the periphery. The axon receives sensory information at the periphery and transmits that information in the form of action potentials to the CNS. With the exception of the bipolar neurons described earlier, most sensory neurons are pseudo-unipolar.

Glial Cells

Glial cells (GLEE-al), or *neuroglia* (nyu-ROH-glee-ah; nerve glue), are the supportive cells of the CNS and PNS, meaning these cells do not conduct action potentials. Instead, glial cells carry out different activities that enhance neuron function and maintain normal conditions within nervous tissue. Glial cells are far more numerous than neurons. Most glial cells retain the ability to divide, whereas neurons do not. The types of glial cells are different in the CNS versus the PNS. In the CNS, there are four types of glial cells. These

include (1) astrocytes, (2) ependymal cells, (3) microglia, and (4) oligodendrocytes. The glial cells of the PNS include (1) Schwann cells and (2) satellite cells.

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Astrocytes (ASS-troh-sites) serve as the major supporting cells in the CNS. In this role, astrocytes can stimulate or inhibit the signaling activity of nearby neurons. In addition, astrocytes participate with the blood vessel endothelium to form a permeability barrier, called the **blood-brain barrier,** between the blood and the CNS. Astrocytes help limit damage to neural tissue; however, the repair process can form a scar that blocks regeneration of damaged axons. **Ependymal** (ep-EN-dih-mal) **cells** line the fluid-filled cavities (ventricles and canals) within the CNS. Some ependymal cells produce cerebrospinal fluid, and others, with cilia, help move the cerebrospinal fluid through the CNS. **Microglia** (my-KROH-glee-ah) act as immune cells of the CNS. They help protect the brain by removing bacteria and cell debris. **Oligodendrocytes** (OL-ih-goh-DEN-droh-sites) provide an insulating material that surrounds axons (figure 8.5 and table 8.1).

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Figure 8.5 APR **Types of Glial Cells**

(*a*) A composite representation of CNS glial cells. (*b*) Astrocytes, with foot processes surrounding a blood capillary. (*c*) Ependymal cells, with cilia extending from the surfaces. (*d*) Microglial cell. (*e*) Oligodendrocyte, forming a myelin sheath around parts of three axons within the CNS. (*f*) Schwann cell forming part of the myelin sheath of an axon in the PNS.

In the PNS, the glial cells known as **Schwann cells** provide insulating material around axons. **Satellite cells** are found around the cell bodies of

certain neurons of the PNS. These cells provide support and nutrition to the neurons and protect the neurons from heavy-metal poisons, such as lead and mercury.

Myelin Sheaths

Myelin sheaths are specialized layers that wrap around the axons of some neurons. These myelin sheaths are formed by the cell processes of oligodendrocytes in the CNS and Schwann cells in the PNS (figure 8.5). Axons with these myelin sheaths are called **myelinated axons** (figure 8.6*a*). Each oligodendrocyte process or Schwann cell repeatedly wraps around a segment of an axon to form a series of tightly wrapped cell membranes. Myelin is an excellent insulator that prevents almost all ion movement across the cell membrane. Gaps in the myelin sheath, called **nodes of Ranvier** (RON-vee-ay), occur about every millimeter between the myelinated areas. Ion movement can occur at the nodes of Ranvier. Myelination of an axon increases the speed and efficiency of action potential generation along the axon. The details of action potentials are described fully in the next section.

Figure 8.6 APR **Comparison of Myelinated and Unmyelinated Axons**

(*a*) Myelinated axon with two Schwann cells forming part of the myelin sheath around a single axon. Each Schwann cell surrounds part of one axon. (*b*) Unmyelinated axons with two Schwann cells surrounding several axons in parallel formation. Each Schwann cell surrounds part of several axons.

Unmyelinated axons lack the myelin sheaths; however, these axons rest in indentations of the oligodendrocytes in the CNS and the Schwann cells in the PNS (figure 8.6*b*). A typical small nerve, which consists of axons of multiple neurons, usually contains more unmyelinated axons than myelinated axons.

Organization of Nervous Tissue

The nervous tissue varies in color due to the location and arrangement of the parts of neurons and glial cells. Nervous tissue exists as gray matter and white matter. **Gray matter** consists of groups of neuron cell bodies and their dendrites, where there is very little myelin. In the CNS, gray matter on the surface of the brain is called the **cortex,** and clusters of gray matter located deeper within the brain are called **nuclei.** Similarly, the PNS contains gray matter. In the PNS, a cluster of neuron cell bodies is called a **ganglion** (GANG-lee-on; pl. ganglia, a swelling or knot).

White matter consists of bundles of parallel axons with their myelin sheaths, which are whitish in color. White matter of the CNS forms **nerve tracts,** or *conduction pathways*, which propagate action potentials from one area of the CNS to another. White matter of the PNS consists of bundles of axons and associated connective tissue that form **nerves.**

8.4 ELECTRICAL SIGNALS AND NEURAL PATHWAYS

Learning Outcomes ***After reading this section, you should be able to***

A. Describe a resting membrane potential.
B. Explain how an action potential is generated and propagated.
C. Compare the roles of leak and gated ion channels.
D. Describe the structure and function of a synapse.
E. Describe a converging and a diverging circuit.
F. Describe the role of summation in neural pathways.

Resting Membrane Potential

Cells of the body have electrical properties. These properties are evident at the cell membrane, a boundary that prevents the free movement of ions into and out of the cell. Recall from chapter 3 that ions cannot move freely across the cell membrane. Instead, because of the cell membrane's hydrophobic interior, ions cross it through ion channels. In part, the flow of ions through these channels is due to their differences in concentration across the membrane. The flow of ions through these channels can also be influenced by their electrical charges, because of the attraction between opposite charges. There are two basic types of ion channels: (1) leak channels and (2) gated channels. **Leak channels** are always open. Thus, ions can "leak" across the membrane, down their concentration gradient. **Gated channels** are closed until opened by specific signals. **Chemically gated channels** are opened by specific chemicals; **voltage-gated channels** are opened by a change in the electrical property of the cell membrane.

When we consider the “sides” of the cell membrane, the inside of most cell membranes is negatively charged compared to the outside of the cell membrane, which is positively charged. This uneven charge distribution across the cell membrane means that the membrane is **polarized.** The inside of the cell membrane can be thought of as the negative pole of a battery and the outside of the cell membrane can be thought of as the positive pole. Thus, a small voltage difference, called the potential, can be measured across the cell membrane. In an unstimulated (or resting) cell, we refer to this as the **resting membrane potential.**

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The resting membrane potential is generated primarily by the uneven distribution of K^+, Na^+, and negatively charged proteins across the cell membrane. Figure 8.7 illustrates the factors that generate the resting membrane potential of a neuron:

PROCESS Figure

PROCESS Figure 8.7 APR Generation of the Resting Membrane Potential

The resting membrane potential results from differences in the concentrations of ions across the membrane and the permeability characteristics of the membrane.

Understand **Though not shown in this figure, Cl^- concentrations are higher outside the cell. However, Cl^- movement across the membrane is limited. Given that the membrane is relatively permeable to Cl^-, explain what factor limits the movement of Cl^- across the membrane.**

❶ *Distribution of ions and proteins across the cell membrane:* In a resting cell, there is a higher concentration of K+ inside the cell and a higher concentration of Na+ outside the cell. It is also important to note that there are more negatively charged proteins inside the cell. Because the cell membrane is not permeable to these proteins, they are isolated in the cytoplasm of the cell and contribute to the negative charge of the inside of the cell membrane.

❷ *Movement of ions through leak channels:* In neurons, there are 50–100 times more K+ leak channels than Na+ leak channels in the cell membrane. As a result, the resting membrane has much greater permeability to K+ than to Na+, which also means that K+ has the greater influence on the resting membrane potential. Because of the ion concentration gradient (described in step 1), K+ diffuses out of the cell, down its concentration gradient, and Na+ diffuses into the cell, down its concentration gradient. Remember that the movement of ions is also influenced by the electrical charge.

Consequently, as positively charged K+ leaks out of the cell via the leak channels, the charge inside the cell membrane becomes even more negative. Because opposite charges are attracted to each other, the negatively charged molecules inside the cell tend to attract the positive K+ back into the cell. As a result, K+ is moving into as well as out of the cell. The resting membrane potential is the point of equilibrium at which the tendency for K+ to move down its concentration gradient out of the cell is balanced by the negative charge within the cell, which tends to attract the K+ back into the cell.

❸ *Sodium-potassium pump maintains resting levels of ions across the cell membrane:* To compensate for the constant leakage of ions across the membrane, the **sodium-potassium pump** (Na+–K+ pump) is required to maintain the greater concentration of Na+ outside the cell and K+ inside the cell. The pump actively transports K+ into the cell and Na+ out of the cell. The importance of this pump is indicated by the astounding

amount of energy it consumes. It is estimated that the sodium-potassium pump consumes 25% of all the ATP in a typical cell and 70% of the ATP in a neuron.

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Neuron Communication

Neurons, as well as muscle cells, are excitable cells, meaning that the resting membrane potential changes in response to stimuli. In muscle cells, this change in the resting membrane potential results in contraction; but in neurons, this change is a means by which the cell communicates with other cells. We can organize our discussion of neuron communication into three stages, as illustrated in figure 8.8:

1. Generation of action potentials,
2. Action potential propagation along the cell membrane, and
3. Communication with target cell at the synapse. We will now review each of these three phases in more detail.

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PROCESS Figure

PROCESS Figure 8.8 APR **Stages of Neuron Communication.**

Neuron communication involves three stages: generation of an action potential, action potential propagation, and communication at the synapse.

Is the illustrated process of Na^+ movement into the neuron a passive process or active process? Explain your answer.

Action Potentials

As stated earlier, the resting membrane potential of a neuron changes in response to stimuli. These stimuli activate gated ion channels. The opening and closing of gated ion channels can change the permeability characteristics of the cell membrane and hence change the membrane potential. In neuron communication, these changes can lead to **action potentials,** electrical signals that are conducted along the cell membrane from one region of the cell to another (figure 8.8, step 1). The channels responsible for the action potential are voltage-gated Na^+ and K^+ channels. Figure 8.9 illustrates the details of action potential generation.

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PROCESS Figure

PROCESS Figure 8.9 APR **Voltage-Gated Ion Channels and the Action Potential**

Step 1 illustrates the status of voltage-gated Na^+ and K^+ channels in a resting cell. Steps 2 and 3 show how the channels open and close to produce an action potential. Next to each step, a graph shows in red the membrane potential resulting from the condition of the ion channels.

Understand **At the end of the action potential sequence, the cell will regain resting concentrations of ions inside the cell. Will this process be active or passive? Explain your answer.**

1. When the cell membrane is at rest, the voltage-gated channels are closed.
2. When a stimulus is applied to a muscle cell or neuron, following neurotransmitter activation of chemically gated channels, Na+ channels open very briefly, and Na+ diffuses quickly into the cell. This movement of Na+, which is called a **local current,** causes the inside of the cell membrane to become positive, a change called **depolarization.** This depolarization results in a **local potential.** If depolarization is not strong enough, the Na+ channels close again, and the local potential disappears without being conducted along the neuron cell membrane. If depolarization is large enough, Na+ enters the cell so that the local potential reaches a **threshold** value. This threshold depolarization causes voltage-gated Na+ channels to open. Threshold is most often reached at the axon hillock, near the cell body. The opening of these channels causes a massive, 600-fold increase in membrane permeability to Na+. Voltage-gated K+ channels also begin to open. As more Na+ enters the neuron, depolarization continues at a much faster pace. Eventually a brief reversal of charge takes place across the cell membrane—the inside of the cell membrane becomes positive relative to the outside of the cell membrane.
3. The charge reversal causes Na+ channels to close and Na+ then stops entering the cell. Also during this time, more K+ channels are opening and K+ leaves the cell. The outward flow of K+ repolarizes the cell membrane to its resting membrane potential.

Depolarization and repolarization constitute an **action potential** (figure 8.10). At the end of repolarization, the charge of the cell membrane briefly becomes more negative than the resting membrane potential; this condition is called **hyperpolarization.** The elevated permeability to K^+ lasts only a very short time.

Figure 8.10 **Action Potential**

Once a local potential reaches threshold, an all-or-none action potential is started. During the depolarization phase, the voltage across the cell membrane changes from approximately −70 mV to approximately +20 mV. During the repolarization phase, the voltage across the cell membrane returns to −70 mV. There is a brief period of hyperpolarization at the end of repolarization before the membrane returns to its resting membrane potential. The entire process lasts 1 or 2 milliseconds (ms).

Apply It 1

Describe the effect of a reduced extracellular concentration of Na^+ on the generation of an action potential in an excitable cell.

In summary, the resting membrane potential is set by the activity of the leak channels. On stimulation, chemically gated channels are opened and initiate *local* potentials. If sufficiently strong, the local potentials activate voltage-gated channels to initiate an *action* potential.

Action potentials occur in an **all-or-none** fashion. That is, if threshold is reached, an action potential occurs; if threshold is not reached, no action potential occurs. Action potentials in a cell are all of the same magnitude—in other words, the amount of charge reversal is always the same. This means that the variation in stimulation is not due to stronger or weaker action potentials, because all action potentials have the same pattern of changes in the membrane potential. Instead, stronger stimuli produce a greater frequency of action potentials. Thus, neural signaling is based on the number of action potentials.

Action Potential Conduction

Once an action potential is generated, it is conducted along the cell membrane (figure 8.8, *step 2*). The pattern of action potential conduction along a neuron cell membrane may occur in one of two ways: (1) continuous conduction or (2) saltatory conduction.

Recall that certain glial cells insulate the axons of neurons, a characteristic called myelination. Action potentials are conducted slowly in unmyelinated axons and more rapidly in myelinated axons. In unmyelinated axons, **continuous conduction** occurs. In this process, an action potential in one part of a cell membrane stimulates local currents in adjacent parts of the cell membrane (figure 8.11*a*). The local currents in the adjacent membrane produce an action potential. By this means, the action potential is conducted along the entire axon cell membrane.

Figure 8.11 **Conduction Along the Axon**

(*a*) During continuous conduction, an action potential in one part of the cell membrane causes local currents in the adjacent membrane, which produce an action potential. (*b*) During saltatory conduction, action potentials occur at successive nodes of Ranvier, resulting in faster propagation compared to continuous conduction.

In myelinated axons, **saltatory** (SAL-tah-tor-ee; to leap) conduction occurs (figure 8.11*b*). In this process, an action potential at one node of Ranvier causes a local current to flow through the surrounding extracellular fluid and

through the cytoplasm of the axon to the next node, stimulating an action potential at that node of Ranvier. By this means, action potentials "jump" from one node of Ranvier to the next along the length of the axon. Saltatory conduction greatly increases the conduction velocity because the nodes of Ranvier make it unnecessary for action potentials to travel along the entire cell membrane. How would you relate the two patterns of action potential conduction to a "real world" example? Here is one analogy. Action potential conduction in a myelinated fiber is like a child skipping across the floor, whereas in an unmyelinated axon it is like a child walking heel to toe across the floor.

The speed of action potential conduction varies widely even among myelinated axons. The variation in speed is explained in part by the difference in axon diameter. Medium-diameter, lightly myelinated axons, characteristic of autonomic neurons, conduct action potentials at the rate of about 3–15 meters per second (m/s), whereas large-diameter, heavily myelinated axons conduct action potentials at the rate of 15–120 m/s. These rapidly conducted action potentials, carried by sensory and motor neurons, allow for rapid responses to changes in the external environment. In addition, several hundred times fewer ions cross the cell membrane during conduction in myelinated cells than in unmyelinated cells. Much less energy is therefore required for the sodium-potassium pump to maintain the ion distribution.

The Synapse

A **synapse** (SIN-aps) is a junction where the axon of one neuron interacts with another neuron or with cells of an effector organ, such as a muscle or gland (figure 8.12; see figure 8.8 *step 3*). When describing the structure of a synapse, we identify three major components: (1) the end of the axon forms a **presynaptic terminal,** (2) the membrane of the dendrite or effector cell is the **postsynaptic membrane,** and (3) the space separating the presynaptic and postsynaptic membranes is the **synaptic cleft.** At most of the synapses in the body, communication between the neuron and its target cell occurs through chemical signals. Chemical substances called **neurotransmitters** (NYUR-oh-trans-MIT-ers; *neuro-,* nerve + *transmitto,* to send across) act as these chemical signals and are stored in **synaptic vesicles** in the presynaptic terminal. Figure 8.12 illustrates the process of communication at the synapse.

PROCESS Figure

PROCESS Figure 8.12 APR The Synapse

A synapse consists of the end of a neuron (presynaptic terminal), a small space (synaptic cleft), and the postsynaptic membrane of another neuron or an effector cell, such as a muscle or gland cell

Understand **Does the movement of Na^+ into the cell shown in step 4 immediately result in an action potential? Why or why not?**

1. When an action potential reaches the presynaptic terminal, voltage-gated Ca^{2+} channels open, and Ca^{2+} moves into the cell.
2. This influx of Ca^{2+} causes the release of neurotransmitters by exocytosis from the presynaptic terminal.
3. The neurotransmitters diffuse across the synaptic cleft toward the postsynaptic membrane.
4. The neurotransmitters then bind to specific receptor molecules on the postsynaptic membrane. The binding of neurotransmitters to these membrane receptors causes chemically gated channels for Na^+, K^+, or Cl^- to open or close in the postsynaptic membrane.

Both the specific channel type and whether or not the channel opens or closes depend on the type of neurotransmitter in the presynaptic terminal and the type of receptors on the postsynaptic membrane. The response may be either stimulation or inhibition of an action potential in the postsynaptic cell. For example, if Na^+ channels open, the postsynaptic cell becomes depolarized, and an action potential will result if threshold is reached, as illustrated in figure 8.12. If K^+ or Cl^- channels open, the inside of the postsynaptic cell tends to become more negative, or **hyperpolarized** (HYE-per-pol-lar-ized), and an action potential is inhibited from occurring.

Of the many neurotransmitters or suspected neurotransmitter substances, the best known are **acetylcholine (ACh)** (AS-eh-til-KOH-leen) and **norepinephrine** (NOR-ep-ih-NEF-rin). See table 8.2 for descriptions of these as well as other neurotransmitters.

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Table 8.2 Neurotransmitters

Substance	Site of Release	Effect	Clinical Example
Acetylcholine (ACh)	CNS synapses, ANS synapses, and neuromuscular junctions	Excitatory or inhibitory	Alzheimer disease (a type of senile dementia) is associated with a decrease in acetylcholine-secreting neurons. Myasthenia gravis (weakness of skeletal muscles) results from a reduction in acetylcholine receptors.

Substance	Site of Release	Effect	Clinical Example
Norepinephrine (NE)	Selected CNS synapses and some ANS synapses	Excitatory	Cocaine and amphetamines increase the release and block the reuptake of norepinephrine, resulting in overstimulation of postsynaptic neurons.
Serotonin	CNS synapses	Generally inhibitory	It is involved with mood, anxiety, and sleep induction. Levels of serotonin are elevated in schizophrenia (delusions, hallucinations, and withdrawal). Drugs that block serotonin transporters, such as Prozac, are used to treat depression and anxiety disorders.
Dopamine	Selected CNS synapses and some ANS synapses	Excitatory or inhibitory	Parkinson disease (depression of voluntary motor control) results from destruction of dopamine-secreting neurons.
Gamma-aminobutyric acid (GABA)	CNS synapses	Inhibitory	Drugs that increase GABA function have been used to treat epilepsy (excessive discharge of neurons).
Glycine	CNS synapses	Inhibitory	Glycine receptors are inhibited by the poison strychnine. Strychnine increases the excitability of certain neurons by blocking their inhibition. Strychnine poisoning results in powerful muscle contractions and convulsions. Tetanus of respiratory muscles can cause death.
Endorphins	Descending pain pathways	Inhibitory	The opiates morphine and heroin bind to endorphin receptors on presynaptic neurons and reduce pain by blocking the release of a neurotransmitter.

Neurotransmitters do not normally remain in the synaptic cleft indefinitely. Thus, their effects on the target cell are typically very short-term. The neurotransmitters become reduced in concentration when they are either rapidly broken down by enzymes within the synaptic cleft or are transported back into the presynaptic terminal. For example, in synapses where acetylcholine is the neurotransmitter, such as in the neuromuscular junction (see chapter 7), an enzyme called **acetylcholinesterase** (AS-eh-til-KOH-

leen-ESS-ter-ase) breaks down the acetylcholine. The breakdown products are then returned to the presynaptic terminal for reuse. Norepinephrine is either actively transported back into the presynaptic terminal or broken down by enzymes. The release and breakdown or removal of neurotransmitters occurs so rapidly that a postsynaptic cell can be stimulated many times a second.

Drugs can modulate the action of neurotransmitters at the synapse. Cocaine and amphetamines increase the release and block the reuptake of norepinephrine, resulting in overstimulation of postsynaptic neurons and deleterious effects on the body. Drugs that block serotonin reuptake are particularly effective at treating depression and behavioral disorders.

Neuronal Pathways

Within the CNS, neurons are organized to form pathways ranging from relatively simple to extremely complex. The two simplest pathways are (1) converging pathways and (2) diverging pathways. In a **converging pathway,** two or more neurons synapse with the same postsynaptic neuron (figure 8.13*a*). This allows information transmitted in more than one neuronal pathway to converge into a single pathway. In a **diverging pathway,** the axon from one neuron divides and synapses with more than one other postsynaptic neuron (figure 8.13*b*). This allows information transmitted in one neuronal pathway to diverge into two or more pathways.

Figure 8.13 **Converging and Diverging Pathways in the Nervous System**
(a) General model of a converging pathway, showing two neurons converging onto one postsynaptic neuron. *(b)* General model of a diverging pathway, showing one neuron diverging onto two postsynaptic neurons.

Within the CNS and in many PNS synapses, it takes more than a single action potential to have an effect. A single presynaptic action potential usually does not cause a sufficiently large postsynaptic local potential to reach threshold and produce an action potential in the target cell. Instead, many presynaptic action potentials are needed in a process called **summation.** Summation of signals in neuronal pathways allows integration of multiple subthreshold local potentials. Summation of the local potentials can bring the membrane potential to threshold and trigger an action potential. There are two types of summation: (1) spatial summation and (2) temporal summation. **Spatial summation** occurs when the local potentials originate from different locations on the postsynaptic neuron—for example, from converging pathways. **Temporal summation** occurs when local potentials overlap in time. This can occur from a single input that fires rapidly, which allows the resulting local potentials to overlap briefly. Spatial and temporal summation can lead to stimulation or inhibition, depending on the type of signal. Collectively, this integration of multiple inputs determines whether the postsynaptic neuron will generate an action potential.

8.5 CENTRAL AND PERIPHERAL NERVOUS SYSTEMS

Learning Outcome ***After reading this section, you should be able to***

A. Compare and contrast the central and peripheral nervous systems.

As mentioned previously, the central nervous system (CNS) consists of the brain and spinal cord (see figure 8.1). The brain is housed within the skull; the spinal cord is in the vertebral column.

The peripheral nervous system (PNS) consists of all the nerves and ganglia outside the brain and spinal cord. The PNS collects information from numerous sources both inside and on the surface of the body and relays it by way of sensory neurons to the CNS, where one of three results is possible: The information is ignored, triggers a reflex, or is evaluated more extensively. Motor neurons in the PNS relay information from the CNS to muscles and glands in various parts of the body, regulating activity in those structures. The nerves of the PNS can be divided into two groups: 12 pairs of cranial nerves and 31 pairs of spinal nerves.

8.6 SPINAL CORD

Learning Outcomes *After reading this section, you should be able to*

A. Describe the relationship between the spinal cord and the spinal nerves.
B. Describe a cross section of the spinal cord.
C. List the parts of a reflex arc, and describe its function.
D. Describe the knee-jerk reflex.
E. Describe the withdrawal reflex.

The **spinal cord** extends from the foramen magnum at the base of the skull to the second lumbar vertebra (figure 8.14). Spinal nerves communicate between the spinal cord and the body. The inferior end of the spinal cord and the spinal nerves exiting there resemble a horse's tail and are collectively called the **cauda equina** (KAW-dah ee-KWI-nah, horse).

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Figure 8.14 APR **Spinal Cord and Spinal Nerve Roots**

The spinal cord extends from the foramen magnum of the skull down to the second lumbar vertebra. The cord is slightly enlarged in the cervical and lumbosacral regions, where the roots of spinal nerves supplying the arms and legs enter and leave the spinal cord.

A cross section reveals that the spinal cord consists of a superficial white matter portion and a deep gray matter portion (figure 8.15*a*). The white matter consists of myelinated axons, and the gray matter is mainly a collection of neuron cell bodies. The white matter in each half of the spinal cord is organized into three columns: (1) the **dorsal** (posterior) **column,** (2) the **ventral** (anterior) **column,** and (3) the **lateral column.** Each column of the spinal cord contains ascending and descending tracts, or pathways. **Ascending tracts** consist of axons that conduct action potentials toward the brain, and **descending tracts** consist of axons that conduct action potentials away from the brain. Ascending tracts and descending tracts are discussed more fully in “Sensory Functions” and “Motor Functions” later in this chapter.

Figure 8.15 APR **Cross Section of the Spinal Cord**
(*a*) In each segment of the spinal cord, rootlets combine to form a dorsal root on the dorsal (posterior) side and a ventral root on the ventral (anterior) side. (*b*) Relationship of sensory and motor neurons to the spinal cord.

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The gray matter of the spinal cord is shaped like the letter H, with **dorsal** (posterior) **horns** and **ventral** (anterior) **horns.** Small **lateral horns** exist in levels of the spinal cord associated with the autonomic nervous system. The **central canal** is a fluid-filled space in the center of the spinal cord.

Spinal nerves arise from numerous rootlets along the dorsal and ventral surfaces of the spinal cord (figure 8.15*a*). The ventral rootlets combine to form a **ventral root** on the ventral (anterior) side of the spinal cord, and the dorsal rootlets combine to form a **dorsal root** on the dorsal (posterior) side

of the spinal cord at each segment. The ventral and dorsal roots unite just lateral to the spinal cord to form a spinal nerve.

The dorsal root has a region called the **dorsal root ganglion** (GANG-lee-on; a swelling or knot). It contains the cell bodies of pseudo-unipolar sensory neurons (figure 8.15*b*). The axons of these neurons originate in the periphery of the body. They pass through spinal nerves and the dorsal roots to the dorsal horn of the spinal cord gray matter. In the dorsal horn, the axons either synapse with interneurons or pass into the white matter and ascend or descend in the spinal cord.

The ventral and lateral horns of the spinal cord gray matter contain the cell bodies of motor neurons, which regulate the activities of muscles and glands. Somatic motor neurons are in the ventral horn, and autonomic neurons are in the lateral horn. Axons from the motor neurons form the ventral roots and pass into the spinal nerves. Thus, the dorsal root contains sensory axons, and the ventral root contains motor axons. Each spinal nerve therefore has both sensory and motor axons.

Understand

Apply It 2

Describe the direction of action potential propagation relative to the CNS in the spinal nerves, dorsal roots, and ventral roots.

Reflexes

A **reflex** is an involuntary reaction in response to a stimulus applied to the periphery and transmitted to the CNS. Reflexes allow a person to react to stimuli more quickly than is possible if conscious thought is involved. A **reflex arc** is the neuronal pathway by which a reflex occurs (figure 8.16). The reflex arc is the basic functional unit of the nervous system because it is the smallest, simplest pathway capable of receiving a stimulus and yielding a response. A reflex arc generally has five basic components:

❶ a **sensory receptor;**

❷ a **sensory neuron;**

❸ in some reflexes, **interneurons,** which are neurons located between and communicating with two other neurons;

❹ a **motor neuron;** and

❺ an **effector organ** (muscles or glands). The simplest reflex arcs do not involve interneurons. Most reflexes occur in the spinal cord or brainstem rather than in the higher brain centers.

PROCESS Figure

PROCESS Figure 8.16 APR **Reflex Arc**

The parts of a reflex arc are labeled in the order in which action potentials pass through them. The five components are the (1) sensory receptor, (2) sensory neuron, (3) interneuron, (4) motor neuron, and (5) effector organ. Simple reflex arcs have only four components because the reflex does not involve interneurons.

Remember **Reflexes can be classified as somatic or autonomic, depending on the effector. Is the reflex illustrated in this figure somatic or autonomic? How do you know?**

Knee-Jerk Reflex

The simplest reflex is the **stretch reflex.** A stretch reflex occurs when muscles contract in response to a stretching force applied to them. The **knee-jerk reflex,** or *patellar reflex,* is a classic example of the stretch reflex involving the spinal cord and is illustrated in figure 8.17.

PROCESS Figure

PROCESS Figure 8.17 **Knee-Jerk Reflex**

The knee-jerk reflex is an example of a stretch reflex whereby the stretching of a muscle stimulates the same muscle to contract.

Stretch reflexes occur in many of the muscles of the body. Using table 7.4, determine which muscles would need to be stretched to cause the upper limb to reflexively bend.

❶ The stimulus for this reflex is stretching of the quadriceps femoris muscle, the extensor muscles. When the patellar ligament is tapped, the quadriceps femoris muscle tendon and the muscles themselves are stretched. Sensory receptors within these muscles are also stretched, and the stretch reflex is activated.

❷ A sensory neuron monitoring the stretch receptor conducts action potentials to the spinal cord.

3. Sensory neurons synapse with motor neurons in the gray matter of the spinal cord segment. Descending neurons within the spinal cord also synapse with the neurons of the stretch reflex, allowing for conscious modification to their activity.
4. Motor neurons from the spinal cord extend to the same muscle of the leg, stimulating them to contract, extending the leg, producing the characteristic knee-jerk response.

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Clinicians use the knee-jerk reflex to determine if the higher CNS centers that normally influence this reflex are functional. Descending neurons within the spinal cord synapse with the neurons of the stretch reflex and modulate their activity. This is an example of a converging pathway. Stretch reflexes are important in maintaining posture and in coordinating muscular activity. Following a severe spinal cord injury, all spinal reflexes are lost below the level of injury. By about 2 weeks after the injury, the knee-jerk reflex returns, but it is often exaggerated. When the stretch reflex is absent or greatly exaggerated, it indicates that the neurons within the brain or spinal cord that modify this reflex have been damaged.

Withdrawal Reflex

The function of the **withdrawal reflex,** or *flexor reflex,* is to remove a limb or another body part from a painful stimulus. The sensory receptors are pain receptors, and stimulation of these receptors initiates the reflex figure 8.18 illustrates the steps of the withdrawal reflex.

PROCESS Figure

PROCESS Figure 8.18 **Withdrawal Reflex**

The withdrawal reflex moves a body part away from a painful stimulus.

Though it is not shown in the figure, another motor neuron in this reflex inhibits the extensor muscles of the limb. Considering what you learned about stretch reflexes, why does this make sense?

1. Painful stimuli initiate action potentials at the pain receptors.
2. The sensory neurons monitoring these receptors conduct action potentials through the dorsal root to the spinal cord.
3. The sensory neurons synapse with interneurons, which in turn synapse with motor neurons.
4. These neurons stimulate muscles, usually flexor muscles, that remove the limb from the source of the painful stimulus.

CLINICAL IMPACT

Spinal Cord Injury

About 10,000 new cases of **spinal cord injury** occur each year in the United States. Automobile and motorcycle accidents are the leading causes, followed by gunshot wounds, falls, and swimming accidents. Most spinal cord injuries are acute contusions (kon-TOO-shuns; bruising) of the cervical portion of the cord and do not completely sever the spinal cord.

Spinal cord injuries can interrupt ascending and/or descending tracts. Reflexes can still function below the level of injury, but sensations and/or motor functions and reflex modulation may be disrupted.

At the time of spinal cord injury, two types of tissue damage occur: (1) primary mechanical damage and (2) secondary tissue damage extending into a much larger region of the cord than the primary damage. The only treatment for primary damage is prevention, such as wearing seat belts when riding in automobiles and not diving in shallow water. Once an accident occurs, however, little can be done about primary damage.

Secondary spinal cord damage, which begins within minutes of the primary damage, is caused by ischemia (lack of blood supply), edema (fluid accumulation), ion imbalances, the release of "excitotoxins" (such as glutamate), and inflammatory cell invasion. Unlike primary damage, much secondary damage can be prevented or reversed if treatment is prompt. Giving the patient large doses of methylprednisolone, a synthetic anti-inflammatory steroid, within 8 hours of the injury can dramatically reduce the secondary damage to the spinal cord. Other treatments include anatomical realignment and stabilization of the vertebral column and decompression of the spinal cord. Rehabilitation is based on retraining the patient to use whatever residual connections exist across the site of damage.

Although the spinal cord was formerly considered incapable of regeneration following severe damage, researchers have learned that most neurons of the adult spinal cord survive an injury and begin to regenerate, growing about 1 mm into the site of damage, before regressing to an inactive, atrophic state. The major block to adult spinal cord regeneration is the formation of a scar, consisting mainly of astrocytes, at the site of injury. Myelin in the scar apparently inhibits regeneration. However, research has shown that implantation of stem cells or other cell types, such as Schwann cells, can bridge the scar and stimulate regeneration. Certain growth factors can also stimulate regeneration. Current research continues to look for the right combination of chemicals and other factors to stimulate regeneration of the spinal cord following injury.

8.7 SPINAL NERVES

Learning Outcome *After reading this section, you should be able to*

A. Define plexus, and describe the three primary plexuses, including their branches.

The **spinal nerves** arise along the spinal cord from the union of the dorsal roots and ventral roots (see figure 8.15). All the spinal nerves contain axons of both sensory and somatic motor neurons and thus are called **mixed nerves.** Some spinal nerves also contain parasympathetic or sympathetic axons. Most of the spinal nerves exit the vertebral column between adjacent vertebrae. Spinal nerves are categorized by the region of the vertebral column from which they emerge—cervical (C), thoracic (T), lumbar (L), sacral (S), and coccygeal (Co). The spinal nerves are also numbered (starting superiorly) according to their order within that region. The 31 pairs of spinal nerves are therefore C1 through C8, T1 through T12, L1 through L5, S1 through S5, and Co (figure 8.19*a*).

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Figure 8.19 APR **Plexuses and Dermatomal Map**

(*a*) Nerves of the spinal cord. The regions are color-coded. (*b*) Dermatomal map of the body. Letters and numbers represent the spinal nerve innervating a region.

The nerves arising from each region of the spinal cord and vertebral column supply specific regions of the body. A **dermatome** is the area of skin supplied with sensory innervation by a pair of spinal nerves. Each of the spinal nerves except C1 has a specific cutaneous sensory distribution. Figure 8.19*b*

illustrates the **dermatomal** (der-mah-TOH-mal) map for the sensory cutaneous distribution of the spinal nerves.

Most of the spinal nerves are organized into three major **plexuses** (PLEK-sus-ez; braids) where neurons of several spinal nerves come together and intermingle. This reorganizes the neurons so that branches of nerves extending from each plexus contain neurons from different spinal segments. The three major plexuses are (1) the cervical plexus, (2) the brachial plexus, and (3) the lumbosacral plexus (table 8.3). The major nerves of the neck and limbs are branches of these plexuses. Spinal nerves T2 through T11 do not join a plexus. Instead, these nerves extend around the thorax between the ribs, giving off branches to muscles and skin. Motor nerve fibers derived from plexuses innervate skeletal muscles, and sensory nerve fibers in those plexuses supply sensory innervation to the skin overlying those muscles (table 8.3). In addition to the major plexuses, the small **coccygeal plexus** supplies motor innervation to the muscles of the pelvic floor and sensory cutaneous innervation to the skin over the coccyx (figure 8.19*b*).

Table 8.3 Plexuses of the Spinal Nerves (see figure 8.19)

Plexus	Origin	Major Nerves	Muscles Innervated	Skin Innervated
Cervical	C1–C4		Several neck muscles	Neck and posterior head
		Phrenic	Diaphragm	
Brachial	C5–T1	Axillary	Two shoulder muscles	Part of shoulder
		Radial	Posterior arm and forearm muscles (extensors)	Posterior arm, forearm, and hand
		Musculocutaneous	Anterior arm muscles (flexors)	Radial surface of forearm
		Ulnar	Two anterior forearm muscles (flexors), most intrinsic hand muscles	Ulnar side of hand
		Median	Most anterior forearm muscles (flexors), some intrinsic hand muscles	Radial side of hand
Lumbosacral	L1–S4	Obturator	Medial thigh muscles (adductors)	Medial thigh

Plexus	Origin	Major Nerves	Muscles Innervated	Skin Innervated
		Femoral	Anterior thigh muscles (extensors)	Anterior thigh, medial leg, and foot
		Tibial	Posterior thigh muscles (flexors), anterior and posterior leg muscles, most foot muscles	Posterior leg and sole of foot
		Common fibular	Lateral thigh and leg, some foot muscles	Anterior and lateral leg, dorsal (top) part of foot
Coccygeal	S5 & Co		Pelvic floor muscles	Skin over coccyx

Cervical Plexus

The **cervical plexus** originates from spinal nerves C1 to C4. Branches from this plexus innervate several of the muscles attached to the hyoid bone, as well as the skin of the neck and posterior portion of the head. One of the most important branches of the cervical plexus is the **phrenic nerve,** which innervates the diaphragm. Contraction of the diaphragm is largely responsible for our ability to breathe (see chapter 15).

Understand ***Apply It 3***

The phrenic nerve may be damaged where it descends along the neck or during open thorax or open heart surgery. Explain how damage to the right phrenic nerve affects the diaphragm. Describe the effect on the diaphragm of completely severing the spinal cord in the thoracic region versus in the upper cervical region.

Brachial Plexus

The **brachial plexus** originates from spinal nerves C5 to T1. Five major nerves emerge from the brachial plexus to supply the upper limb and shoulder. The **axillary nerve** innervates two shoulder muscles and the skin over part of the shoulder. The **radial nerve** innervates all the muscles in the posterior arm and forearm as well as the skin over the posterior surface of the arm, forearm, and hand.

The radial nerve lies very close to the medial side of the humerus in the proximal part of the arm and is susceptible to damage in that area. If a person uses crutches improperly so that the weight of the body is borne in the axilla and upper arm rather than by the hands, the top of the crutch can compress the radial nerve against the humerus. This compression can cause dysfunction of the radial nerve, resulting in paralysis of the posterior arm and forearm muscles and loss of sensation over the back of the forearm and hand. This condition, known as "crutch paralysis," subsides if the patient begins to use the crutches correctly.

The **musculocutaneous** (MUS-kyoo-loh-kyoo-TAY-nee-us; muscle + skin) **nerve** innervates the anterior muscles of the arm and the skin over the radial surface of the forearm. The **ulnar nerve** innervates two anterior forearm muscles and most of the intrinsic hand muscles. It also innervates the skin over the ulnar side of the hand. The ulnar nerve can be easily damaged where it passes posterior to the medial side of the elbow. The ulnar nerve at this location is called the "funny bone." The **median nerve** innervates most of the anterior forearm muscles and some of the intrinsic hand muscles. It also innervates the skin over the radial side of the hand.

Lumbosacral Plexus

The **lumbosacral** (LUM-boh-SAY-kral) **plexus** originates from spinal nerves L1 to S4. Four major nerves exit the lumbrosacral plexus to supply the lower limb. The **obturator** (OB-tour-ah-tor; OB-tour-ate-or) **nerve** innervates the muscles of the medial thigh and the skin over the same region. The **femoral nerve** innervates the anterior thigh muscles and the skin over the anterior thigh and medial side of the leg. The **tibial nerve** innervates the posterior thigh muscles, the anterior and posterior leg muscles, and most of the intrinsic foot muscles. It also innervates the skin over the sole of the foot. The **common fibular** (FIB-yoo-lar) **nerve** innervates the muscles of the lateral thigh and leg and some intrinsic foot muscles. It also innervates the skin over the anterior and lateral leg and the dorsal surface (top) of the foot. The tibial and common fibular nerves are bound together within a connective tissue sheath and together are called the **sciatic** (sigh-AT-ik) **nerve.**

8.8 BRAIN

Learning Outcomes ***After reading this section, you should be able to***

A. List the parts of the brain.
B. List the parts of the brainstem, and state their functions.
C. State where the cerebellum is located.

D. List the parts of the diencephalon, and state their functions.

E. List the lobes of the cerebrum, and state a function for each.

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The major regions of the brain are (1) the brainstem, (2) the cerebellum, (3) the diencephalon, and (4) the cerebrum (figure 8.20).

Figure 8.20 APR **Regions of the Right Half of the Brain**

Medial view of a midsagittal section of the right half of the brain.

Dennis Strete/McGraw-Hill Education

Brainstem

The **brainstem** connects the spinal cord to the remainder of the brain (figure 8.21). It consists of three parts: (1) the medulla oblongata, (2) the pons, and (3) the midbrain. The brainstem contains several nuclei involved in vital body functions, such as the control of heart rate, blood pressure, and breathing. Damage to small areas of the brainstem can cause death, whereas damage to relatively large areas of the cerebrum or cerebellum often do not. Nuclei for all but the first two cranial nerves are also located in the brainstem.

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Figure 8.21 APR **Brainstem and Diencephalon**

(*a*) Anterior view of the brainstem. (*b*) Posterolateral view. The inset shows the location of the diencephalon and brainstem.

Medulla Oblongata

The **medulla oblongata** (ob-lon-GAH-tah) is the most inferior portion of the brainstem (figure 8.21) and is continuous with the spinal cord. It extends superiorly from the level of the foramen magnum to the pons. The medulla oblongata contains ascending and descending nerve tracts, which convey signals to and from other regions of the brain. In addition, the medulla oblongata contains discrete nuclei with specific functions, such as regulation of heart rate and blood vessel diameter, breathing, swallowing, vomiting, coughing, sneezing, balance, and coordination.

On the anterior surface of the medulla oblongata are two prominent enlargements called **pyramids** (figure 8.21*a*). The pyramids consist of descending nerve tracts, which transmit action potentials from the brain to somatic motor neurons of the spinal cord and are involved in the conscious control of skeletal muscles.

Apply **Apply It 4**

*A large tumor or **hematoma** (hee-mah-TOH-mah), a mass of blood that occurs as the result of bleeding into the tissues, can cause increased pressure within the skull. This pressure can force the medulla oblongata downward toward the foramen magnum. The displacement can compress the medulla oblongata and lead to death. Give two likely causes of death, and explain why they would occur.*

Pons

Immediately superior to the medulla oblongata is the **pons** (PONZ; bridge). It contains ascending and descending nerve tracts, as well as several nuclei. Some of the nuclei in the pons relay information between the cerebrum and the cerebellum. Not only is the pons a functional bridge between the cerebrum and cerebellum, but on the anterior surface it resembles an arched footbridge (figure 8.21*a*). Several nuclei of the medulla oblongata, described earlier, extend into the lower part of the pons, so functions such as breathing, swallowing, and balance are controlled in the lower pons, as well as in the medulla oblongata. Other nuclei in the pons control functions such as chewing and salivation.

Midbrain

The **midbrain,** just superior to the pons, is the smallest region of the brainstem (figure 8.21*b*). The dorsal part of the midbrain consists of four mounds of tissue called the **colliculi** (koh-LIK-you-lie; sing. colliculus, hill). The two inferior colliculi are major relay centers for the auditory nerve pathways in the CNS. The two superior colliculi are involved in visual reflexes and receive touch and auditory input. Turning the head toward a tap on the shoulder, a sudden loud noise, or a bright flash of light is a reflex controlled in the superior colliculi. The midbrain contains nuclei involved in coordinating eye movements and controlling pupil diameter and lens shape. The midbrain also contains a black nuclear mass, called the **substantia nigra** (sub-STAN-shee-ah NYE-grah; black substance), which is part of the basal nuclei (see "Basal Nuclei" in section 8.10) and is involved in regulating general body movements. The rest of the midbrain consists largely of ascending tracts from the spinal cord to the cerebrum and descending tracts from the cerebrum to the spinal cord or cerebellum.

Reticular Formation

Scattered throughout the brainstem is a group of nuclei collectively called the **reticular formation.** The reticular formation plays important regulatory functions. It is particularly involved in regulating cyclical motor functions, such as respiration, walking, and chewing. The reticular formation is a major

component of the **reticular activating system,** which plays an important role in arousing and maintaining consciousness and in regulating the sleep-wake cycle. Stimuli such as a ringing alarm clock, sudden bright lights, smelling salts, or cold water splashed on the face can arouse consciousness. Conversely, removal of visual or auditory stimuli may lead to drowsiness or sleep. General anesthetics suppress the reticular activating system. Damage to cells of the reticular formation can cause coma.

Cerebellum

The **cerebellum** (ser-eh-BELL-um; little brain), shown in figure 8.20, is attached to the brainstem by several large connections called **cerebellar peduncles** (pe-DUNG-kuhls; *pes,* foot). These connections provide routes of communication between the cerebellum and other parts of the CNS. The structure and function of the cerebellum are discussed in "Motor Functions" later in this chapter.

Diencephalon

The **diencephalon** (die-en-SEF-a-lon) is the part of the brain between the brainstem and the cerebrum (figure 8.22). Its main components are (1) the thalamus, (2) the epithalamus, and (3) the hypothalamus.

Figure 8.22 APR **Diencephalon**

(*a*) Median section of the diencephalon showing the thalamus, epithalamus, and hypothalamus. (*b*) Both halves of the thalamus as seen from an anterior, dorsolateral view with the separations between nuclei depicted by indentations on the surface.

Thalamus

The **thalamus** (THAL-ah-mus) is by far the largest part of the diencephalon. It consists of a cluster of nuclei and is shaped somewhat like a yo-yo, with two large, lateral parts connected in the center by a small **interthalamic adhesion** (figure 8.22*b*). Most sensory input that ascends through the spinal cord and brainstem projects to the thalamus. Within the thalamus, ascending neurons synapse with thalamic neurons, which in turn send their axons to the cerebral cortex. The thalamus also influences mood and registers an unlocalized, uncomfortable perception of pain.

Epithalamus

The **epithalamus** (ep-ih-THAL-ah-mus; *epi,* upon) is a small area superior and posterior to the thalamus (figure 8.22). It consists of a few small nuclei, which are involved in the emotional and visceral response to odors, and the pineal gland. The **pineal** (PIN-ee-al; pinecone-shaped) **gland** is an endocrine gland that may influence the onset of puberty and may play a role in controlling some long-term cycles that are influenced by the light-dark cycle. In animals, the pineal gland is known to influence annual behaviors, such as migration in birds, as well as changes in the color and density of fur in some mammals (see chapter 10).

Hypothalamus

The **hypothalamus** is the most inferior part of the diencephalon; it contains several small nuclei that are very important in maintaining homeostasis. The hypothalamus plays a central role in the control of body temperature, hunger, and thirst. Sensations such as sexual pleasure, rage, fear, and relaxation after a meal are related to hypothalamic functions. Emotional responses that seem inappropriate to the circumstances, such as “nervous perspiration” or “emotional eating,” also involve the hypothalamus. A funnel-shaped stalk, the **infundibulum** (IN-fun-DIB-you-lum; a funnel), extends from the floor of the hypothalamus to the pituitary gland. The hypothalamus plays a major role in controlling the secretion of hormones from the pituitary gland (see chapter 10). The **mammillary** (MAM-ih-lar-ee; *mamilla,* nipple) **bodies** form externally visible swellings on the posterior portion of the hypothalamus. The mammillary bodies are involved in emotional responses to odors and in memory.

Cerebrum

The **cerebrum** (ser-EE-brum; brain) is the largest part of the brain (figure 8.23). It is divided into left and right hemispheres by a **longitudinal fissure.** The most conspicuous features on the surface of each hemisphere are numerous folds called **gyri** (JY-ree. gyrus, *gyros,* circle) and intervening grooves called **sulci** (SUL-kee; sing. sulcus, a furrow or ditch). The gyri greatly increase the surface area of the cerebral cortex.

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Figure 8.23 APR **Cerebrum**

(*a*) Superior view of the two hemispheres of the cerebrum. (*b*) Lateral view of the left cerebral hemisphere, showing the lobes.

(a) ©R. T. Hutchings; (b) Rebecca Gray/McGraw-Hill Education

Each cerebral hemisphere is divided into lobes, which are named for the skull bones overlying them.

1. The **frontal lobe** is important in the control of voluntary motor functions, motivation, aggression, mood, and olfactory (smell) reception.
2. The **parietal lobe** is the principal center for receiving and consciously perceiving most sensory information, such as touch, pain, temperature, and balance. The frontal and parietal lobes are separated by the **central sulcus.**
3. The **occipital lobe** functions in receiving and perceiving visual input and is not distinctly separate from the other lobes.
4. The **temporal lobe** (figure 8.23*b*) is involved in olfactory (smell) and auditory (hearing) sensations and plays an important role in memory. Its anterior and inferior portions, called the "psychic cortex," are associated with functions such as abstract thought and judgment. Most of the temporal lobe is separated from the rest of the cerebrum by the **lateral fissure.**
5. Deep within the lateral fissure is the **insula** (IN-soo-lah), often referred to as the fifth lobe, which is involved in the perception of taste (see chapter 9).

8.9 SENSORY FUNCTIONS

Learning Outcomes ***After reading this section, you should be able to***

A. List the major ascending tracts.
B. State a function for each of the major ascending tracts.
C. Describe the sensory and association areas of the cerebral cortex.
D. Discuss the interactions between the sensory and association areas of the cerebral cortex.

The CNS constantly receives a variety of stimuli originating both inside and outside the body. We are unaware of a large part of this sensory input, but it

is vital to our survival and normal functions. Sensory input to the brainstem and diencephalon helps maintain homeostasis. Input to the cerebrum and cerebellum keeps us informed about our environment and allows the CNS to control motor functions. A small portion of the sensory input results in **perception,** the conscious awareness of stimuli (see chapter 9).

Ascending Tracts

The spinal cord and brainstem contain a number of **ascending** (sensory) **tracts,** or pathways, that transmit information via action potentials from the periphery to various parts of the brain (table 8.4 and figure 8.24). Each tract is involved with a limited type of sensory input, such as pain, temperature, touch, position, or pressure, because each tract contains axons from specific sensory receptors specialized to detect a particular type of stimulus (see chapter 9).

Table 8.4 Ascending Tracts (see figures 8.24 and 8.25)

Pathway	Function
Spinothalamic	Pain, temperature, light touch,pressure, tickle, and itch sensations
Dorsal column	Proprioception, touch, deep pressure, and vibration
Spinocerebellar (anterior and posterior)	Proprioception to cerebellum

Figure 8.24 **Ascending Tracts of the Spinal Cord**
Ascending pathways are highlighted and labeled on the left side of the figure only, although they exist on both sides.

Tracts are usually given composite names that indicate their origin and termination. The names of ascending tracts usually begin with the prefix *spino-,* indicating that they begin in the spinal cord. For example, the spinothalamic tract begins in the spinal cord and terminates in the thalamus.

Most ascending tracts consist of two or three neurons in sequence, from the periphery to the brain. Almost all neurons relaying information to the cerebrum terminate in the thalamus. Another neuron then relays the information from the thalamus to the cerebral cortex. Two examples of ascending tracts are (1) the spinothalamic tract and (2) the dorsal column tract. The **spinothalamic tract** transmits action potentials dealing with sensations such as pain and temperature to the thalamus and on to the cerebral cortex. The **dorsal column** transmits action potentials dealing with sensations such as touch, pressure, and **proprioception,** or body position (figure 8.25 and table 8.4).

Figure 8.25 **Dorsal Column**

The dorsal column transmits action potentials dealing with touch, proprioception, and pressure. Lines on the inset indicate levels of section.

Sensory tracts typically cross from one side of the body in the spinal cord or brainstem to the other side of the body. Thus, the left side of the brain receives sensory input from the right side of the body, and vice versa.

Ascending tracts also terminate in the brainstem or cerebellum. The anterior and posterior **spinocerebellar tracts,** for example, transmit information about proprioception to the cerebellum (see "Cerebellum" in section 8.10).

Sensory Areas of the Cerebral Cortex

Figure 8.26 depicts a lateral view of the left cerebral cortex with some of the sensory and motor areas indicated. The terms *area* and *cortex* are often used interchangeably for these regions of the cerebral cortex. Ascending tracts project to specific regions of the cerebral cortex, called **primary sensory areas,** where sensations are perceived. The **primary somatosensory cortex,** or *general sensory area,* is located in the parietal lobe posterior to the central sulcus. Sensory fibers carrying general sensory input, such as pain, pressure, and temperature, synapse in the thalamus, and thalamic neurons relay the information to the primary somatosensory cortex. Sensory fibers from specific parts of the body project to specific regions of the primary somatosensory cortex so that a topographic map of the body, with the head most inferior, exists in this part of the cerebral cortex (figure 8.26). Other primary sensory areas include the visual cortex in the occipital lobe, the primary auditory cortex in the temporal lobe, and the taste area in the insula.

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Figure 8.26 **Sensory and Motor Areas of the Lateral Side of the Left Cerebral Cortex**
Sensory and motor areas are indicated by different colors. Notice the body areas associated with specific regions of the primary motor cortex and primary sensory cortex.

Cortical areas immediately adjacent to the primary sensory areas, called **association areas,** are involved in the process of recognition. For example, sensory action potentials originating in the retina of the eye reach the visual

cortex, where the image is perceived. Action potentials then pass from the visual cortex to the visual association area, where the present visual information is compared to past visual experience ("Have I seen this before?"). On the basis of this comparison, the visual association area "decides" whether the visual input is recognized and judges whether the input is significant. For example, if you pass a man walking down a street, you usually pay less attention to him if you've never seen him before than if you know him, unless a unique characteristic of the unknown person draws your attention. Other examples of association areas are the auditory association area, adjacent to the primary auditory cortex, and the somatosensory association area, adjacent to the primary somatosensory cortex.

8.10 SOMATIC MOTOR FUNCTIONS

Learning Outcomes *After reading this section, you should be able to*

A. Describe the somatic motor area of the cerebral cortex.
B. Discuss how the somatic motor area interacts with other parts of the frontal lobe.
C. Distinguish between upper and lower somatic motor neurons.
D. Distinguish between direct and indirect tracts.
E. Discuss how the basal nuclei and cerebellum regulate somatic motor functions.

The somatic motor system of the brain and spinal cord is responsible for maintaining the body's posture and balance, as well as moving the trunk, head, limbs, tongue, and eyes. In addition, the somatic motor system allows us to communicate through facial expressions and speech. Reflexes mediated through the spinal cord and brainstem are responsible for some body movements. These are called **involuntary movements** because they occur without conscious thought. **Voluntary movements,** on the other hand, are consciously activated to achieve a specific goal, such as walking or typing. Although consciously activated, the details of most voluntary movements occur automatically. For example, once you start walking, you don't have to think about the moment-to-moment control of every muscle because neural circuits in the reticular formation and spinal cord automatically control your limbs. Once learned, complex tasks, such as typing, can be performed relatively automatically.

Voluntary movements result from the stimulation of neural circuits that consist of two motor neurons: (1) upper motor neurons and (2) lower motor neurons. **Upper motor neurons** have cell bodies in the cerebral cortex. The axons of upper motor neurons form descending tracts that connect to lower motor neurons. **Lower motor neurons** have cell bodies in the ventral (anterior) horn of the spinal cord gray matter or in cranial nerve nuclei. The

axons of lower motor neurons leave the central nervous system and extend through spinal or cranial nerves to skeletal muscles. Lower motor neurons form the motor units described in chapter 7.

Motor Areas of the Cerebral Cortex

The **primary motor cortex** is located in the posterior portion of the frontal lobe, directly anterior to the central sulcus (figure 8.26). Action potentials initiated in this region control voluntary movements of skeletal muscles. Upper motor neuron axons project from specific regions of this cortex to specific parts of the body so that a topographic map of the body exists in the primary motor cortex, with the head inferior, analogous to the topographic map of the primary somatosensory cortex (figure 8.26). The **premotor area** of the frontal lobe is where motor functions are organized before they are actually initiated in the primary motor cortex. For example, if a person decides to take a step, the neurons of the premotor area are first stimulated, and the determination is made there as to which muscles must contract, in what order, and to what degree. Action potentials are then passed to the upper motor neurons of the primary motor cortex, which initiate each planned movement.

The motivation and foresight to plan and initiate movements occur in the anterior portion of the frontal lobes, called the **prefrontal area.** This region of association cortex is well developed only in primates, especially humans. It is involved in motivation and regulation of emotional behavior and mood. The large size of this area in humans may account for our emotional complexity and our relatively well-developed capacity to think ahead and feel motivated.

Descending Tracts

The names of the descending tracts are based on where they originate in the brain and where they terminate in the spinal cord or the brainstem (table 8.5 and figure 8.27). For example, the corticospinal tracts are so named because they begin in the cerebral cortex and terminate in the spinal cord. The corticospinal tracts are considered **direct** because they extend directly from upper motor neurons in the cerebral cortex to lower motor neurons in the spinal cord (a similar direct tract extends to lower motor neurons in the brainstem). Other tracts are named after the part of the brainstem from which they originate. Although they originate in the brainstem, these tracts are indirectly controlled by the cerebral cortex, basal nuclei, and cerebellum. These tracts are called **indirect** because no direct connection exists between the cortical and spinal neurons.

Table 8.5 Descending Tracts (see figures 8.27 and 8.28)	
Pathway	**Function**
Direct	
Lateral corticospinal	Muscle tone and skilled movements, especially of hands
Anterior corticospinal	Muscle tone and movement of trunk muscles
Indirect	
Rubrospinal	Movement coordination
Reticulospinal	Posture adjustment, especially during movement
Vestibulospinal	Posture and balance
Tectospinal	Movement in response to visual reflexes

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Figure 8.27 **Descending Tracts of the Spinal Cord**
Descending pathways (*indicated with bold labels*) are highlighted and labeled on the left side of the figure only, although they exist on both sides.

The descending tracts control different types of movements (table 8.5). Tracts in the lateral columns (see figure 8.15; figure 8.27) are most important in controlling goal-directed limb movements, such as reaching and manipulating. The **lateral corticospinal tracts** are especially important in controlling the speed and precision of skilled movements of the hands. Tracts in the ventral columns, such as the reticulospinal tract, are most important for maintaining posture, balance, and limb position through their control of neck, trunk, and proximal limb muscles.

The lateral corticospinal tract serves as an example of how descending pathways function. It begins in the cerebral cortex and descends into the brainstem (figure 8.28). At the inferior end of the pyramids of the medulla oblongata, the axons cross over to the opposite side of the body and continue into the spinal cord. Crossover of axons in the brainstem or spinal cord to the opposite side of the body is typical of descending pathways. Thus, the left side of the brain controls skeletal muscles on the right side of the body, and vice versa. The upper motor neuron synapses with interneurons that then synapse with lower motor neurons in the brainstem or spinal cord. The axon of the lower motor neuron extends to the skeletal muscle fiber.

Figure 8.28 **Example of a Direct Tract**

The lateral corticospinal tract is responsible for movement below the head. Lines on the inset indicate levels of section.

Basal Nuclei

The **basal nuclei** are a group of functionally related nuclei (figure 8.29). Two primary nuclei are (1) the **corpus striatum** (KOR-pus stry-AH-tum), located deep within the cerebrum, and (2) the **substantia nigra,** a group of darkly pigmented cells in the midbrain.

Figure 8.29 **Basal Nuclei**
The basal nuclei are a functional grouping of nuclei important to coordinating movement and maintaining posture.

The basal nuclei are important in planning, organizing, and coordinating motor movements and posture. Complex neural circuits link the basal nuclei with each other, with the thalamus, and with the cerebral cortex. These connections form several feedback loops, some of which are stimulatory and others inhibitory. The stimulatory circuits facilitate muscle activity, especially at the beginning of a voluntary movement, such as rising from a sitting position or beginning to walk. The inhibitory circuits facilitate the actions of the stimulatory circuits by inhibiting muscle activity in antagonist muscles. In addition, inhibitory circuits inhibit random movements of the trunk and limbs. Inhibitory circuits also decrease muscle tone when the body, limbs, and head are at rest. Disorders of the basal nuclei result in difficulty rising from a sitting position and difficulty initiating walking. People with basal nuclei disorders exhibit increased muscle tone and exaggerated, uncontrolled movements when they are at rest. A specific feature of some basal nuclei disorders is “resting tremor,” a slight shaking of the hands when a person is not performing a task. Parkinson disease, Huntington disease, and cerebral

palsy are basal nuclei disorders (see table 8.9, Representative Diseases and Disorders, in the Systems Pathology feature near the end of this chapter).

Cerebellum

The **cerebellum** is attached by cerebellar peduncles to the brainstem (see figures 8.21 and 8.23*b*). The cerebellar cortex is composed of gray matter and has gyri and sulci, but the gyri are much smaller than those of the cerebrum. Internally, the cerebellum consists of gray nuclei and white nerve tracts. The cerebellum is involved in maintaining balance and muscle tone and in coordinating fine motor movement. If the cerebellum is damaged, muscle tone decreases, and fine motor movements become very clumsy.

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A major function of the cerebellum is that of a **comparator** (figure 8.30). A comparator is a sensing device that compares the data from two sources—in this case, the motor cortex and peripheral structures. Figure 8.30 illustrates the comparator function of the cerebellum.

PROCESS Figure

PROCESS Figure 8.30 **Cerebellar Comparator Function**

The cerebellar comparator ensures smooth and coordinated skeletal muscle movement by comparing intended movements with sensory information from actively moving body parts.

A kicker on the local football team has experienced head trauma. When attempting to kick the ball, his movements were jerky and exaggerated. The team's athletic trainer was convinced that the kicker had damage to his cerebellum and insisted that he be transported to the hospital. Does the athletic trainer's conclusion make sense? Why or why not?

❶ Action potentials from the cerebral motor cortex descend into the spinal cord, synapsing with lower motor neurons to initiate voluntary movements.

❷ Collateral branches are also sent from the motor cortex to the cerebellum, providing information representing the intended movement.

❸ In addition, simultaneously, reaching the cerebellum are action potentials from **proprioceptive** (proh-pree-oh-SEP-tive) **neurons,** which

innervate joints, tendons, and muscles and provide information about the position of body parts.

4. The cerebellum compares information about the intended movement from the motor cortex to sensory information from the moving structures.
5. If a difference is detected, the cerebellum sends action potentials to motor neurons in the motor cortex and the spinal cord to correct the discrepancy.

The result of the cerebellar comparator function is smooth and coordinated movements. For example, if you close your eyes, the cerebellar comparator function allows you to touch your nose smoothly and easily with your finger. If the cerebellum is not functioning, your finger tends to overshoot the target. One effect of alcohol is to inhibit the function of the cerebellum.

Another function of the cerebellum involves participating with the cerebrum in learning motor skills, such as playing the piano. Once the cerebrum and cerebellum "learn" these skills, the specialized movements can be accomplished smoothly and automatically.

8.11 OTHER BRAIN FUNCTIONS

Learning Outcomes *After reading this section, you should be able to*

A. Discuss the right and left cerebral hemispheres and speech.

B. Compare and contrast the features of working, short-term, and the two types of long-term memory.

Communication Between the Right and Left Hemispheres

The right cerebral hemisphere receives sensory input from and controls muscular activity in the left half of the body. The left cerebral hemisphere receives input from and controls muscles in the right half of the body. Sensory information received by one hemisphere is shared with the other through connections between the two hemispheres called **commissures** (KOM-mih-shurz; joining together). The largest of these commissures is the **corpus callosum** (KOR-pus kah-LOH-sum), a broad band of nerve tracts at the base of the longitudinal fissure (see figures 8.20 and 8.22).

Language and perhaps other functions, such as artistic activities, are not shared equally between the two hemispheres. Researchers believe the left hemisphere is the more analytical hemisphere, emphasizing such skills as mathematics and speech, whereas the right hemisphere is more involved in functions such as three-dimensional or spatial perception and musical ability.

Speech

In most people, the speech area is in the left cerebral cortex. Two major cortical areas are involved in speech: (1) The **sensory speech area** (Wernicke area), located in the parietal lobe, functions in understanding and formulating coherent speech. (2) The **motor speech area** (Broca area), located in the frontal lobe, controls the movement necessary for speech (see figure 8.26). Damage to these parts of the brain or to associated brain regions may result in **aphasia** (ah-FAY-zee-ah; *a-,* without + *phasis,* speech), absent or defective speech or language comprehension. The most common cause of aphasia is a stroke. It is estimated that 25–40% of stroke survivors exhibit aphasia.

Speech-related functions involve both sensory and motor pathways. For example, to repeat a word that you *hear* involves the following sequence of events: (1) Action potentials from the ear reach the primary auditory cortex, where the word is perceived. (2) The word is recognized in the auditory association area and comprehended in portions of the sensory speech area. (3) Action potentials representing the word are then conducted through nerve tracts that connect the sensory and motor speech areas. (4) In the motor speech area, the muscle activity needed to repeat the word is determined. (5) Action potentials then go to the premotor area, where the movements are programmed. (6) Finally, action potentials are conducted to the primary motor cortex, where specific movements are triggered.

Speaking a *written* word involves a slightly different pathway: (1) The information enters the visual cortex, then passes to the visual association area, where it is recognized. (2) The information continues to the sensory speech area, where it is understood and formulated as it is to be spoken. From the sensory speech area, it follows the same route for repeating words that you hear: (3) through nerve tracts to the motor speech area, (4) to the premotor area, and (5) then to the primary motor cortex.

Apply It 5

Describe a neural pathway that allows a blindfolded person to name an object placed in her hand.

Brain Waves and Consciousness

Different levels of consciousness can be revealed by different patterns of electrical activity in the brain. Electrodes placed on a person's scalp and attached to a recording device can record the brain's electrical activity, producing an **electroencephalogram** (eh-LEK-troh-en-SEF-ah-loh-gram) **(EEG)** (figure 8.31). These electrodes are not positioned so that they can

detect individual action potentials, but they can detect the simultaneous action potentials in large numbers of neurons. Most of the time, EEG patterns are irregular, with no particular pattern, because the brain's electrical activity is normally not synchronous. At other times, however, EEG patterns can be detected as wavelike patterns known as **brain waves.** Their intensity and frequency differ, based on the state of brain activity. The different levels of consciousness in an awake and a sleeping person are marked by different types of brain waves. **Alpha waves** are observed in a normal person who is awake but in a quiet, resting state with the eyes closed. **Beta waves** have a higher frequency than alpha waves and occur during intense mental activity. During the beginning of sleep, a rapid transition takes place from a beta rhythm to an alpha rhythm. As sleep deepens, progressively more delta waves occur. **Delta waves** occur during deep sleep, in infants, and in patients with severe brain disorders. A fourth type of brain waves, **theta waves,** are usually observed in children, but they can also occur in adults who are experiencing frustration or who have certain brain disorders. Neurologists use these patterns to diagnose and determine the treatment for the disorders.

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Figure 8.31 **Electroencephalogram**

(*a*) Patient with electrodes attached to her head. (*b*) Four electroencephalographic tracings.

(a) PHANIE/Science Source

Memory

The storage of memory can be divided into three stages: (1) working, (2) short-term, and (3) long-term. Long-term memories can also be subdivided

based on the type of the memory: (a) those dealing with facts (*declarative*) and (b) those dealing with skills (*procedural*).

The brain briefly stores information required for the immediate performance of a task. This task-associated memory is called **working memory.** It lasts only a few seconds to minutes and occurs mostly in the frontal cortex. Working memory is limited primarily by the number of bits of information (about seven) that can be stored at any one time. When new information is presented, old information, previously stored in working memory, is eliminated. What happens to a telephone number you just looked up if you are distracted?

Short-term memory lasts longer than working memory and can be retained for a few minutes to a few days. Short-term memories are stored by a mechanism involving increased synaptic transmission. Short-term memory is susceptible to brain trauma, such as physical injury or decreased oxygen, and to certain drugs that affect neural function, such as general anesthetics.

Short-term memory is transferred to **long-term memory,** where it may be stored for only a few minutes or become permanent, by **consolidation,** a gradual process involving the formation of new and stronger synaptic connections. The length of time memory is stored may depend on how often it is retrieved and used. **Declarative memory,** or *explicit memory,* involves the retention of facts, such as names, dates, and places, as well as related emotional undertones. Emotion and mood apparently serve as gates in the brain and determine what is stored in long-term declarative memory. **Procedural memory,** or *reflexive memory,* involves the development of motor skills, such as riding a bicycle. Only a small amount of procedural memory is lost over time.

Long-term memory involves structural and functional changes in neurons that lead to long-term enhancement of synaptic transmission. A whole series of neurons, called **memory engrams,** or *memory traces,* are probably involved in the long-term retention of a given piece of information, a thought, or an idea. Repeating the information and associating it with existing memories help us transfer information from short-term to long-term memory.

Limbic System and Emotions

The olfactory cortex and certain deep cortical regions and nuclei of the cerebrum and the diencephalon are grouped together under the title **limbic** (LIM-bic; a boundary) **system** (figure 8.32). The limbic system influences long-term declarative memory, emotions, visceral responses to emotions, motivation, and mood. A major source of sensory input to the limbic system

is the olfactory nerves. The limbic system responds to olfactory stimulation by initiating responses necessary for survival, such as hunger and thirst. The limbic system is connected to, and functionally associated with, the hypothalamus. Lesions in the limbic system can result in voracious appetite, increased (often perverse) sexual activity, and docility (including loss of normal fear and anger responses).

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Figure 8.32 **Limbic System**

The limbic system includes the olfactory cortex, the cingulate gyrus (an area of the cerebral cortex on the medial side of each hemisphere), nuclei such as those of the hypothalamus and thalamus, the hippocampus (a mass of neuron cell bodies in the temporal lobe), and connecting nerve tracts, such as the fornix.

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MICROBES IN YOUR BODY

Brain Function: Is It Affected by Our Gut Microbiota?

Most of us would agree that our mental state can affect our health. For example, many students often find themselves "coming down with something" just about the time midterm or final exams are happening. This can be explained by the fact that stress hormones depress our immune system. But is the opposite connection true? Would

most people agree that our brain's function, and perhaps even its development, can be influenced by the health of another organ in our body?

In today's medical world, we're on the cusp of a paradigm shift. Surprising new evidence suggests that certain central nervous system diseases are linked to our gut microbiota population. Moreover, evidence suggests that there is bidirectional signaling between the gut and the brain, via a gut-brain axis. This might mean that simply adjusting the gut microbe population can help treat disorders such as depression and anxiety.

There is a growing body of data from both human and mouse studies that supports the notion of a gut-brain axis. In humans, disorders of the gut, such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD), occur in conjunction with high levels of anxiety. Treatment of IBS/IBD patients with probiotics, supplemental bacteria that foster further gut bacterial growth, has been useful in minimizing the symptoms of these disorders. Similarly, patients suffering from chronic liver disease experience a complication called hepatic encephalopathy, which decreases cognition. When untreated, these patients have elevated serum levels of gut microbe–specific short-chain fatty acids. These short-chain fatty acids induce autism-like behavior; however, upon antibiotic treatment and reduced levels of these short-chain fatty acids, patients regain normal cognition. Further, autism patients also experience benefits from antibiotic treatment, albeit temporarily.

In mice studies, the connection between behavior and gut microbiota is becoming well established. For example, numerous studies with naturally bacteria-free mice, called germ-free mice, have demonstrated a relationship between stress and anxiety-related behaviors and gut microbiota populations. Germ-free mice have higher stress and anxiety levels, which are decreased upon colonization with normal gut microbiota. In fact, calm mice become anxious when they receive transplants of gut microbiota from already anxious mice. The reverse is also true. In addition, scientists have examined indicators of brain function, such as levels of the molecule brain-derived neurotrophic factor (BDNF), an important regulator of multiple cognitive and emotional behaviors. BDNF is crucial for supporting neuronal survival and increasing the growth of new neurons and synapses. Germ-free mice produce less BDNF than do mice with normal gut microbiota. In particular, limbic system structures, including the hippocampus, hypothalamus, and amygdala, produce lower levels of BDNF in germ-free mice. Upon colonization of germ-free mice with gut microbiota, BDNF levels return to normal.

There is much more work to be done to completely unravel the mystery of the gut-brain axis. However, there is clearly a developing link between cognition and emotional behaviors and gut microbiota.

Apply It 6

You learned that IBS/IBD patients, among others, tend to have higher levels of anxiety when their condition goes untreated. You also learned that gut bacteria produce short-chain fatty acids, which can enter the blood plasma in levels sufficient enough to be measured by a clinical test. It is thought that these short-chain fatty acids are responsible for inducing the anxiety experienced by IBS/IBD patients. Propose a mechanism by which the short-chain fatty acids might communicate with the areas in the brain that regulate anxiety.

8.12 MENINGES, VENTRICLES, AND CEREBROSPINAL FLUID

Learning Outcomes *After reading this section, you should be able to*

A. Describe the three meningeal layers surrounding the central nervous system.
B. Describe the four ventricles of the brain.
C. Explain the origin and circulation of the cerebrospinal fluid.

Meninges

Three connective tissue membranes, the **meninges** (meh-NIN-jeez; *meninx,* membrane) (figure 8.33), surround and protect the brain and spinal cord. The meninges include (1) the dura mater, (2) the arachnoid mater, and (3) the pia mater.

Figure 8.33 APR **Meninges**

(*a*) Anterior superior view of the head to show the meninges. (*b*) Meningeal membranes surrounding the spinal cord. (*c*) Cross section of a vertebra and the spinal cord.

The most superficial and thickest of the meninges is the **dura mater** (DYU-rah MAY-ter; tough mother). The dura mater around the brain consists of two layers, which are in contact over much of their surface. However, in some areas, the two layers separate to form dural folds and dural venous

sinuses. Folds of dura mater extend into the longitudinal fissure between the two cerebral hemispheres and between the cerebrum and the cerebellum. The folds help hold the brain in place within the skull. The dural venous sinuses collect blood from the small veins of the brain and empty into the internal jugular veins, which exit the skull.

Damage to the veins crossing between the cerebral cortex and the dural venous sinuses can cause bleeding into the subdural space, resulting in a **subdural hematoma,** which can put pressure on the brain. The pressure can result in decreased brain function in the affected area. For example, the primary motor cortex is located in the posterior portion of the frontal lobe. Therefore, pressure on the portion of the right primary motor cortex involved in hand movements can cause decreased function in the left hand. The frontal lobe is also involved with mood; thus, pressure in that area can result in mood changes—for example, a normally happy person may become irritable. Subdural hematoma is more common in people over age 60 because their veins are less resilient and more easily damaged.

Within the skull, the dura mater adheres tightly to the cranial bones. Within the vertebral canal, however, there is an **epidural space** between the dura mater and the vertebrae (figure 8.33*c*). The epidural space of the vertebral canal is clinically important as the injection site for **epidural anesthesia** of the spinal nerves, which is often given to females during childbirth.

The second meningeal membrane is the very thin, wispy **arachnoid mater** (ah-RAK-noyd MA-ter; spiderlike, as in cobwebs)**.** The space between the dura mater and the arachnoid mater is the **subdural space,** which is normally only a potential space containing a very small amount of serous fluid.

The spinal cord extends only to approximately the level of the second lumbar vertebra. Spinal nerves surrounded by meninges extend to the end of the vertebral column. Because there is no spinal cord in the inferior portion of the vertebral canal, a needle can be introduced into the subarachnoid space at that level without damaging the spinal cord. Health professionals use such a needle to inject anesthetic into the area as a **spinal block** or to take a sample of cerebrospinal fluid in a **spinal tap.** The cerebrospinal fluid can then be examined for infectious agents (meningitis) or for blood (hemorrhage).

The third meningeal membrane, the **pia mater** (PEE-ah MAY-ter; affectionate mother), is very tightly bound to the surface of the brain and spinal cord. Between the arachnoid mater and the pia mater is the **subarachnoid space,** which is filled with cerebrospinal fluid and contains blood vessels.

Ventricles

The CNS contains fluid-filled cavities, called **ventricles,** which are quite small in some areas and large in others (figure 8.34). Each cerebral hemisphere contains a relatively large cavity called the **lateral ventricle.** The **third ventricle** is a smaller, midline cavity located in the center of the diencephalon between the two halves of the thalamus and connected by foramina (holes) to the lateral ventricles. The **fourth ventricle** is located at the base of the cerebellum and connected to the third ventricle by a narrow canal, called the **cerebral aqueduct.** The fourth ventricle is continuous with the **central canal** of the spinal cord. The fourth ventricle also opens into the subarachnoid space through foramina in its walls and roof.

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Figure 8.34 APR **Ventricles of the Brain Viewed from the Left**

The ventricles contain cerebrospinal fluid produced by the choroid plexuses.

Cerebrospinal Fluid

Cerebrospinal fluid (CSF) bathes the brain and spinal cord, providing a protective cushion around the CNS. The **choroid** (KOR-oid; lacy) **plexuses** produce the CSF. These plexuses are specialized structures located in the ventricles and composed of ependymal cells. CSF fills the brain ventricles, the

central canal of the spinal cord, and the subarachnoid space. Figure 8.35 illustrates the flow of CSF within the brain.

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PROCESS Figure

PROCESS Figure 8.35 APR **Flow of CSF**

White arrows indicate the direction of CSF flow, and *black arrows* indicate the direction of blood flow in the sinuses.

Analyze **Hydrocephalus occurs when CSF accumulates in the ventricles and passageways of the brain. Assuming that CSF production is normal, propose reasons for the accumulation of the fluid.**

❶ CSF is produced by the choroid plexuses of the ventricles.

❷ The CSF flows from the lateral ventricles into the third ventricle.

❸ CSF then flows through the cerebral aqueduct into the fourth ventricle.

❹ The CSF exits the fourth ventricle through small openings in its walls and roof and enters the subarachnoid space. A small amount of CSF enters the central canal of the spinal cord.

❺ Masses of arachnoid tissue, called **arachnoid granulations,** penetrate the superior sagittal sinus, a dural venous sinus in the longitudinal fissure, and CSF passes from the subarachnoid space into the blood through these granulations.

Blockage of the openings in the fourth ventricle or the cerebral aqueduct can cause CSF to accumulate in the ventricles, a condition known as **hydrocephalus.** The accumulation of fluid creates increased pressure that dilates the ventricles and compresses the brain tissue, which usually results in irreversible brain damage. If the skull bones are not completely ossified when the hydrocephalus occurs, as in a fetus or newborn, the pressure can also cause severe enlargement of the head. Hydrocephalus is treated by placing a drainage tube (shunt) from the ventricles to the abdominal cavity to eliminate the high internal pressures.

8.13 CRANIAL NERVES

Learning Outcome *After reading this section, you should be able to*

A. List the various types of cranial nerves, and briefly describe their functions.

The 12 pairs of **cranial nerves** are listed in table 8.6 and pictured in figure 8.36. They are designated by Roman numerals from I to XII. There are two general categories of cranial nerve function: sensory and motor. Sensory functions can be divided into the special senses, such as vision, and the more general senses, such as touch and pain in the face. Motor functions are subdivided into somatic motor and parasympathetic. Somatic motor cranial nerves innervate skeletal muscles in the head and neck. Parasympathetic

cranial nerves innervate glands, smooth muscle throughout the body, and cardiac muscle of the heart.

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Table 8.6 Cranial Nerves and Their Functions (see figure 8.36)

Number	Name	General Function*	Specific Function
I	Olfactory	S	Smell
II	Optic	S	Vision
III	Oculomotor	M, P	Motor to four of six extrinsic eye muscles and upper eyelid; parasympathetic: constricts pupil, thickens lens
IV	Trochlear	M	Motor to one extrinsic eye muscle
V	Trigeminal	S, M	Sensory to face and teeth; motor to muscles of mastication (chewing)
VI	Abducens	M	Motor to one extrinsic eye muscle
VII	Facial	S, M, P	Sensory: taste; motor to muscles of facial expression; parasympathetic to salivary andtear glands
VIII	Vestibulocochlear	S	Hearing and balance
IX	Glossopharyngeal	S, M, P	Sensory: taste and touch to back of tongue; motor to pharyngeal muscles;parasympathetic to salivary glands
X	Vagus	S, M, P	Sensory to pharynx, larynx, and viscera; motor to palate, pharynx, and larynx; parasympathetic to viscera of thorax and abdomen
XI	Accessory	M	Motor to two neck and upper back muscles
XII	Hypoglossal	M	Motor to tongue muscles

*S, sensory; M, somatic motor; P, parasympathetic

Figure 8.36 APR **Inferior Surface of the Brain Showing the Origin of the Cranial Nerves**

The cranial nerves transmit and relay information to and from the brain.

Neurons associated with cranial nerves include sensory neurons, somatic motor neurons, and parasympathetic neurons of the autonomic nervous system. Some cranial nerves are only sensory, and some are only somatic motor, whereas other cranial nerves are mixed nerves with sensory, somatic motor, and parasympathetic functions. Three cranial nerves—the olfactory, optic, and vestibulocochlear nerves—are sensory only. Four other cranial nerves—the trochlear, abducens, accessory, and hypoglossal nerves—are considered somatic motor only (although these motor nerves do provide proprioceptive information).

The trigeminal nerve has sensory and somatic motor functions. It has the greatest general sensory distribution of all the cranial nerves and is the only cranial nerve supplying sensory information to the brain from the skin of the face. Sensory information from the skin over the rest of the body is carried to the CNS by spinal nerves. Injections of anesthetic by a dentist are designed to block sensory transmission through branches of the trigeminal nerve from

the teeth. These dental branches of the trigeminal nerve are probably anesthetized more often than any other nerves in the body.

The oculomotor nerve is somatic motor and parasympathetic. The facial, glossopharyngeal, and vagus nerves have all three functions: sensory, somatic motor, and parasympathetic (table 8.6). The vagus nerve is probably the most important parasympathetic nerve in the body. It helps regulate the functions of the thoracic and abdominal organs, such as heart rate, respiration rate, and digestion.

As with the spinal nerves, the sensory and motor functions of many cranial nerves cross from one side of the head or body to the opposite side of the cerebral cortex. For example, sensory input from the right side of the face via the trigeminal nerve (V) crosses in the brainstem and projects to the left cerebral cortex. Motor output from the left cerebral cortex crosses in the brainstem to the right side of the face via the facial nerve (VII).

8.14 AUTONOMIC NERVOUS SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Contrast the structure of the autonomic nervous system and the somatic motor system.

B. Name the two divisions of the autonomic nervous system, and describe the anatomical and neurotransmitter differences between them.

C. Compare and contrast the general functions of the parasympathetic and sympathetic nervous systems.

The autonomic nervous system (ANS) comprises motor neurons that carry action potentials from the CNS to the periphery. The autonomic neurons innervate smooth muscle, cardiac muscle, and glands. Autonomic functions are largely controlled unconsciously.

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Recall that in the somatic motor pathways, lower motor neurons extend from the CNS to the skeletal muscle. In the autonomic nervous system, two neurons in series extend from the CNS to the effector organs. The first neuron is called the **preganglionic neuron;** the second neuron is the **postganglionic neuron** (figure 8.37). The neurons are so named because preganglionic neurons synapse with postganglionic neurons in **autonomic ganglia** within the PNS. An exception is the preganglionic neuron that extends to the adrenal gland. There, the postganglionic neurons are actually the hormone-secreting cells of the adrenal medulla.

Figure 8.37 **Organization of Somatic and Autonomic Nervous System Neurons**

(*a*) The cell body of the somatic motor neuron is in the CNS, and its axon extends to the skeletal muscle. (*b*) The cell body of the preganglionic neuron is in the CNS, and its axon extends to the autonomic ganglion and synapses with the postganglionic neuron. The postganglionic neuron extends to and synapses with its effector organ.

The autonomic nervous system is composed of the **sympathetic** (sim-pah-THET-ik; *sympatheo,* to feel with + *pathos,* suffering) **division** and the **parasympathetic** (payr-ah-sim-pah-THET-ik; *para,* alongside of) **division** (table 8.7 and figure 8.38). Increased activity in sympathetic neurons generally prepares the individual for physical activity, whereas parasympathetic stimulation generally activates involuntary functions, such as digestion, that are normally associated with the body at rest.

Table 8.7 Sympathetic and Parasympathetic Divisions of the Autonomic Nervous System (see figure 8.38)

Division	Location of Preganglionic Cell Body	Location of Postganglionic Cell Body	General Function
Sympathetic	T1–L2	Sympathetic chain ganglia or collateral ganglia	"Fight-or-flight"; prepares the body for physical activity
Parasympathetic	Cranial nerves III, VII, IX, X; S2–S4 spinal nerves	Terminal ganglia near or embedded in the walls of target organs	"Rest-and-digest"; stimulates involuntaryactivities of the body at rest

Figure 8.38 APR **Innervation of Organs by the ANS**

Preganglionic fibers are indicated by *solid lines*, and postganglionic fibers are indicated by *dashed lines*.

Anatomy of the Sympathetic Division

Cell bodies of sympathetic preganglionic neurons are in the lateral horn of the spinal cord gray matter (see figure 8.15) between the first thoracic (T1) and the second lumbar (L2) segments. The axons of the preganglionic neurons exit through ventral roots and project to either sympathetic chain ganglia or collateral ganglia (figure 8.38). The **sympathetic chain ganglia** are

connected to one another and are so named because they form a chain along both sides of the spinal cord. Some preganglionic fibers synapse with postganglionic fibers in the sympathetic chain ganglia. The postganglionic axons form sympathetic nerves that innervate structures of the thoracic cavity. The axons of those preganglionic fibers that do not synapse in the sympathetic chain ganglia form **splanchnic nerves** that extend to collateral ganglia. **Collateral ganglia** are located nearer target organs. The collateral ganglia include the celiac, superior mesenteric, and inferior mesenteric ganglia. Preganglionic neurons synapse with postganglionic neurons in the collateral ganglia. Postganglionic neurons in the collateral ganglia project to target tissues in the abdominal and pelvic regions.

Anatomy of the Parasympathetic Division

Preganglionic cell bodies of the parasympathetic division are located either within brainstem nuclei of the oculomotor nerve (III), facial nerve (VII), glossopharyngeal nerve (IX), or vagus nerve (X) or within the lateral part of the central gray matter of the spinal cord in the regions that give rise to spinal nerves S2 through S4.

Axons of the preganglionic neurons extend through spinal nerves or cranial nerves to **terminal ganglia** either located near effector organs in the head (figure 8.38) or embedded in the walls of effector organs in the thorax, abdomen, and pelvis. The axons of the postganglionic neurons extend a relatively short distance from the terminal ganglia to the target organ. Most of the thoracic and abdominal organs are supplied by preganglionic neurons of the **vagus nerve** extending from the brainstem. The vagus nerve branches to provide parasympathetic innervation to the heart, the lungs, the liver, and the stomach and other digestive organs.

Autonomic Neurotransmitters

The neurotransmitters of the autonomic nervous system vary depending on the specific synapse. All preganglionic neurons of both the sympathetic and the parasympathetic divisions and all the postganglionic neurons of the parasympathetic division secrete the neurotransmitter **acetylcholine.** Most postganglionic neurons of the sympathetic division secrete **norepinephrine.** Many body functions can be stimulated or inhibited by drugs that either mimic these neurotransmitters or prevent the neurotransmitters from activating their target tissues.

Functions of the Autonomic Nervous System

The sympathetic (**fight-or-flight**) division of the autonomic nervous system prepares a person for physical activity (table 8.8). These actions include increasing heart rate and blood pressure, dilating respiratory passageways to increase airflow, and stimulating the release of glucose from the liver for energy. At the same time, it inhibits digestive activities. In this way, the sympathetic division decreases the activity of organs not essential for the maintenance of physical activity and shunts blood and nutrients to structures that are active during exercise. In addition, excess heat is removed by vasodilation of the vessels near the skin and increased perspiration. The sympathetic division is referred to as the "fight-or-flight" system because it prepares the person either to stand and face a threat or to leave the situation as quickly as possible.

Table 8.8 Effects of the ANS on Various Tissues

Target	Sympathetic Effects	Parasympathetic Effects
Heart	Increases rate and force of contraction	Decreases rate
Blood vessels	Constricts and dilates	None
Lungs	Dilates bronchioles	Constricts bronchioles
Eyes	Dilates pupil, relaxes ciliary muscle to adjust lens for far vision	Constricts pupil, contracts ciliary muscle to adjust lens for near vision
Intestinal and stomach walls	Decreases motility, contracts sphincters	Increases motility, relaxes sphincters
Liver	Breaks down glycogen, releases glucose	Synthesizes glycogen
Adipose tissue	Breaks down lipids	None
Adrenal gland	Secretes epinephrine, norepinephrine	None
Sweat glands	Secretes sweat	None
Salivary glands	Secretes thick saliva	Secretes watery saliva
Urinary bladder	Relaxes muscle, constricts sphincter	Contracts muscle, relaxes sphincter

Target	Sympathetic Effects	Parasympathetic Effects
Pancreas	Decreases secretion of digestive enzymes and insulin	Increases secretion of digestive enzymes and insulin

The parasympathetic division **(rest-and-digest)** of the autonomic nervous system is generally consistent with resting conditions (table 8.8). Increased activity of the parasympathetic division stimulates involuntary activities, such as digestion, defecation, and urination. The actions of the parasympathetic division in the digestive system illustrate how the ANS can coordinate the activities of multiple organs. Parasympathetic activity causes the release of digestive enzymes from the pancreas and contractions to mix the enzymes with food in the small intestine and move the material through the digestive tract. This cooperativity enhances the digestion and absorption of food. At the same time, parasympathetic stimulation lowers heart rate, which lowers blood pressure, and constricts air passageways, which decreases airflow.

The sympathetic and parasympathetic divisions can each produce both stimulatory and inhibitory effects, depending on the target tissue. For example, the sympathetic division stimulates smooth muscle contraction in blood vessel walls and inhibits smooth muscle contraction in lung airway walls. Likewise, the parasympathetic division stimulates contraction of the urinary bladder and inhibits contraction of the heart.

Most organs that receive autonomic neurons are innervated by both the parasympathetic and the sympathetic division, a phenomenon known as **dual innervation.** In most cases, the two autonomic divisions affect the target organs in opposite ways. For example, sympathetic stimulation of the heart causes an increase in heart rate, whereas parasympathetic stimulation causes a decrease in heart rate. When both divisions innervate a single organ, the sympathetic division tends to play a major role during physical activity or stress, whereas the parasympathetic division has more influence during resting conditions. Despite the general opposing actions of the two divisions, in some situations, both divisions can act together to coordinate the activity of multiple targets. For example, in males, the parasympathetic division initiates erection of the penis, and the sympathetic division stimulates the release of secretions and helps initiate ejaculation. Not all organs receive dual innervation. Sweat glands and blood vessels are innervated by sympathetic neurons almost exclusively, whereas the smooth muscles associated with the lens of the eye are innervated primarily by parasympathetic neurons.

Understand **Apply It 7**

List some of the responses stimulated by the autonomic nervous system in (a) a person who is extremely angry and (b) a person who has just finished eating and is now relaxing.

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SYSTEMS PATHOLOGY

Stroke

Background Information

Scott is 45 years old. He is overweight, has high blood pressure, and spends a lot of time watching TV, eating, and smoking. One day, Scott began to feel drowsy and his vision was blurry. He tried to stand up but felt dizzy. He vomited and collapsed to the floor, unconscious. At the hospital, Scott exhibited weakness in his limbs, especially on the right side; ataxia; loss of feeling of pain and temperature in his right leg and the left side of his face; disorientation and lack of attentiveness; hoarseness and dysphagia (inability to swallow); nystagmus (rhythmic oscillation of the eyes); slightly dilated pupils; short and shallow respiration; and elevated pulse rate and blood pressure. (See figure 8.39 for additional effects of stroke.)

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Figure 8.39 Systems Interactions: Stroke

A stroke can have negative effects on many areas of the body. The diagram illustrates how the systems of the body are affected following a stroke.

Scott had suffered a "stroke," also referred to as a **cerebrovascular accident (CVA).** The term **stroke** describes a heterogeneous group of conditions involving the death of brain tissue due to disruption of its vascular supply. There are two types of stroke: **Hemorrhagic stroke** results from bleeding of arteries supplying brain tissue, and **ischemic** (is-KEE-mik) **stroke** results when arteries supplying brain tissue are blocked (figure 8.40). The blockage in ischemic stroke can result from a thrombus, which is a clot that develops in place within an artery, or an embolism, which is a plug composed of a detached thrombus or other foreign body, such as a fat globule or gas bubble, that becomes lodged in an artery, blocking it. Scott's age, lifestyle and smoking caused him to be at high risk of developing a stroke.

Figure 8.40 Brain Images of Stroke Victims

(*a*) MRI (magnetic resonance imaging) of a massive stroke in the left side (the viewer's right) of the brain. (*b*) Colorized NMR (nuclear magnetic resonance) showing disruption of blood flow to the left side of the brain (*yellow*). This disruption could cause a stroke.

(a) Medical Body Scans/Science Source; (b) CNRI/Science Source

The combination of motor loss (as exhibited by weakness in the limbs) and sensory loss (evidenced by loss of pain and temperature sensation in the left lower limb and loss of all sensation in the right side of the face), along with the ataxia, dizziness, nystagmus, and hoarseness, suggests that the stroke affected the brainstem and cerebellum. Blockage of the vertebral artery, a major artery supplying the brain or its branches, can result in an area of dead tissue called a lateral medullary infarction. Damage to the descending motor tracts in that area, above the medullary crossover point, causes muscle weakness. Damage to ascending tracts can result in loss of pain and temperature sensation or other sensory modalities, depending on the affected tract. Damage to cranial nerve nuclei causes the loss of pain and temperature sensation in the face, dizziness, blurred vision, nystagmus, vomiting, and hoarseness. These signs and symptoms are not observed unless the lesion is in the brainstem, where these nuclei are located. Some damage to the cerebellum, also supplied by branches of the vertebral artery, can account for the ataxia.

General responses to neurological damage include drowsiness, disorientation, inattentiveness, loss of consciousness, and even seizures. Depression, due to either neurological damage or discouragement, is also common. Slight dilation of the pupils, short and shallow respiration, and increased pulse rate and blood pressure are all signs of Scott's anxiety about his current condition and his immediate future. Because he lost consciousness, Scott would not remember the last few minutes of what he was watching on television when he had his stroke. People in these circumstances are often worried about how they are going to deal with work tomorrow. They often have no idea that the motor and sensory losses may be permanent or that a long stretch of therapy and rehabilitation lies ahead.

Table 8.9 REPRESENTATIVE DISEASES AND DISORDERS: Nervous System	
Condition	**Description**

Condition	Description
	CENTRAL NERVOUS SYSTEM DISORDERS
Encephalitis	Inflammation of the brain caused by a virus and less often by bacteria or other agents; symptoms include fever, coma, and convulsions
Meningitis	Inflammation of meninges caused by viral or bacterial infection; symptoms include stiffness in the neck, headache, and fever; severe cases can cause paralysis, coma, or death
Multiple sclerosis	Autoimmune condition; may be initiated by viral infection; inflammation in brain and spinal cord with demyelination and sclerotic (hard) sheaths results in poor conduction of action potentials; symptoms include exaggerated reflexes, tremor, and speech defects
Parkinson disease	Caused by a lesion in basal nuclei; characterized by muscular rigidity, resting tremor, general lack of movement, and a slow, shuffling gait
Alzheimer disease	Mental deterioration, or dementia; usually affects older people; involves loss of neurons in cerebral cortex; symptomsinclude general intellectual deficiency, memory loss, short attention span, moodiness, disorientation, and irritability
	PERIPHERAL NERVOUS SYSTEM DISORDERS
General PNS Disorders	
Herpes	Family of diseases characterized by skin lesions due to herpes viruses in sensory ganglia; different viruses cause oral lesions (cold sores), sexually transmitted disease with lesions on genitalia, or chickenpox in children (shingles in adults)
Poliomyelitis	Viral infection of the CNS; damages somatic motor neurons, leaving muscles without innervation, and leads to paralysis and atrophy
Myasthenia gravis	Autoimmune disorder affecting acetylcholine receptors; makes the neuromuscular junction less functional; muscle weakness and increased fatigue lead to paralysis

Apply It 7

Given that Scott exhibited weakness in his right limbs and loss of pain and temperature sensation in his right lower limb and the left side of his face, which side of the brainstem was most severely affected by the stroke? Explain your answer.

CLINICAL IMPACT

Biofeedback and Meditation

Biofeedback is a technique that uses electronic instruments or other methods to monitor subconscious activities, many of which are regulated by the autonomic nervous system. For example, skin temperature, heart rate, and brain waves may be monitored electronically. Then, by watching the monitor and using biofeedback techniques, a person can learn to consciously reduce his or her heart rate and blood pressure or change the pattern of brain waves. The severity of peptic (stomach) ulcers, migraine headaches, high blood pressure, anxiety, or depression can be reduced by using biofeedback techniques.

Meditation is another technique that influences autonomic functions. Its practitioners also claim that meditation can improve their spiritual well-being, consciousness, and holistic view of the universe. Some people find meditation techniques useful in reducing heart rate, blood pressure, the severity of ulcers, and other symptoms frequently associated with stress.

8.15 ENTERIC NERVOUS SYSTEM

Learning Outcome *After reading this section, you should be able to*

A. Discuss how the enteric nervous system can act independently of the CNS.

The **enteric nervous system (ENS)** consists of plexuses within the wall of the digestive tract (see figure 16.2). The plexuses include (1) sensory neurons that connect the digestive tract to the CNS; (2) sympathetic and parasympathetic neurons that connect the CNS to the digestive tract; and (3) enteric neurons, located entirely within the enteric plexuses. A unique feature of enteric neurons is that they are capable of monitoring and controlling the digestive tract independently of the CNS through local reflexes. For example, stretching of the digestive tract is detected by enteric sensory neurons, which stimulate enteric interneurons. The enteric interneurons stimulate enteric motor neurons, which stimulate glands to secrete. Although the ENS is capable of controlling the activities of the digestive tract completely independently of the CNS, normally the two systems work together. CNS control of parasympathetic branches of the vagus nerve and sympathetic nerves (primarily, the splanchnic nerves) can override the actions of enteric

neurons. Hence, the ENS is an independent subdivision of the PNS that is integrated with the ANS.

EFFECTS OF AGING ON THE NERVOUS SYSTEM

As a person ages, sensory and motor functions gradually decline because of decreases in the number of sensory neurons, reduced function of the remaining neurons, and decreased CNS processing. These declines alter an individual's sensory perception and motor abilities, both of which can lead to injury. Examples of sensory dysfunction associated with aging include reduced skin sensitivity to touch or pressure, as well as loss of proprioception.

Other examples of sensory neurons with reduced function include those that monitor blood pressure, thirst, objects in the throat, the amount of urine in the urinary bladder, and the amount of feces in the rectum. As a result, elderly people are more prone to high blood pressure, dehydration, swallowing and choking problems, urinary incontinence, and constipation or bowel incontinence.

A general decline in the number of motor neurons also occurs. As many as 50% of the lower motor neurons in the lumbar region of the spinal cord may be lost by age 60. Muscle fibers innervated by the lost motor neurons are also lost, resulting in a general decline in muscle mass. Loss of motor units leads to more rapid fatigue as the remaining units must perform compensatory work. However, regular physical exercise can forestall and reduce these declines.

Reflexes slow as people age. As reflexes slow, older people are less able to react automatically, quickly, and accurately to changes in internal and external conditions.

The size and weight of the brain decrease as a person ages. At least part of these changes results from the loss of neurons within the cerebrum. The remaining neurons can apparently compensate for much of this loss. Structural changes also occur in neurons and at the synapses between neurons. These changes reduce neuron function and thus brain function, such as short-term memory, problem solving, and planning.

Many of these changes are affected by a person’s background, education, health, motivation, and experience. It appears that continued mental activity can decrease the loss of mental skills with aging.

Older people tend to require more time to fall asleep and experience more periods of waking during the night, which are also of greater duration. Factors that can affect sleep include pain,

indigestion, rhythmic leg movements, sleep apnea, decreased urinary bladder capacity, and poor peripheral circulation.

SUMMARY

8.1 Functions of the Nervous System

The functions of the nervous system include receiving sensory input, integrating information, controlling muscles and glands, maintaining homeostasis, and serving as the center of mental activity.

8.2 Divisions of the Nervous System

1. The central nervous system (CNS) consists of the brain and spinal cord, whereas the peripheral nervous system (PNS) consists of all the nervous tissue outside the CNS.
2. The sensory division of the PNS transmits action potentials to the CNS; the motor division carries action potentials away from the CNS.
3. The motor division is divided into somatic and autonomic systems. The somatic motor system innervates skeletal muscle and is mostly under voluntary control. The autonomic nervous system innervates cardiac muscle, smooth muscle, and glands and is mostly under involuntary control.
4. The autonomic nervous system is divided into sympathetic and parasympathetic divisions.
5. The enteric nervous system contains both sensory and motor neurons, which can function independently of the CNS.

8.3 Cells of the Nervous System

Neurons

1. Neurons receive stimuli and conduct action potentials. A neuron consists of a cell body, dendrites, and an axon.
2. Neurons are multipolar, bipolar, or pseudo-unipolar.

Glial Cells

Glial cells are the support cells of the nervous system. They include astrocytes, ependymal cells, microglia, oligodendrocytes, and Schwann cells.

Myelin Sheaths

Axons are either unmyelinated or myelinated.

Organization of Nervous Tissue

Nervous tissue consists of white matter and gray matter. Gray matter forms the cortex and nuclei in the brain and ganglia in the PNS. White matter forms nerve tracts in the CNS and nerves in the PNS.

8.4 Electrical Signals and Neural Pathways

Resting Membrane Potential

1. A resting membrane potential results from the charge difference across the membrane of cells.
2. The resting membrane potential is set by leak ion channels and the sodium-potassium pump.

Neuron Communication

1. The process of neuron communication can be described in three parts: (1) generation of action potentials, (2) action potential propagation along the cell membrane, (3) communication at the synapse.
2. An action potential occurs when the charge across the cell membrane is briefly reversed.
3. Chemically gated and voltage-gated ion channels generate the action potential.
4. Continuous conduction occurs along unmyelinated axons.
5. Saltatory conduction occurs along myelinated axons.
6. A synapse is a point of contact between two neurons or between a neuron and another cell, such as a muscle or gland cell.
7. An action potential arriving at the synapse causes the release of a neurotransmitter from the presynaptic terminal, which diffuses across the synaptic cleft and binds to the receptors of the postsynaptic membrane.

Neuronal Pathways

1. Neuronal pathways are either converging or diverging.
2. Spatial and temporal summation occur in neuronal pathways.

8.5 Central and Peripheral Nervous Systems

The CNS consists of the brain and spinal cord. The PNS consists of nerves and ganglia outside the CNS.

8.6 Spinal Cord

1. The spinal cord extends from the foramen magnum to the second lumbar vertebra; below that is the cauda equina.
2. The spinal cord has a central gray part organized into horns and a peripheral white part forming nerve tracts.
3. Roots of spinal nerves extend out of the cord.

Reflexes

1. Reflex arcs are the functional units of the nervous system.
2. A complex reflex arc consists of a sensory receptor, a sensory neuron, interneurons, a motor neuron, and an effector organ; the simplest reflex arcs do not involve interneurons.
3. The knee-jerk reflex occurs when the quadriceps femoris muscle is stretched.
4. The withdrawal reflex removes a body part from a painful stimulus.

8.7 Spinal Nerves

1. The spinal nerves exit the vertebral column at the cervical, thoracic, lumbar, and sacral regions.
2. The nerves are grouped into plexuses.
3. The phrenic nerve, which supplies the diaphragm, is the most important branch of the cervical plexus.
4. The brachial plexus supplies nerves to the upper limb.
5. The lumbosacral plexus supplies nerves to the lower limb.

8.8 Brain

Brainstem

1. The brainstem contains several nuclei.

2. The medulla oblongata contains nuclei that control activities such as heart rate, breathing, swallowing, and balance.
3. The pons contains relay nuclei between the cerebrum and cerebellum.
4. The midbrain is involved in hearing and in visual reflexes.
5. The reticular formation is scattered throughout the brainstem and is important in regulating cyclical motor functions. It is also involved in maintaining consciousness and in the sleep-wake cycle.

Cerebellum

The cerebellum is attached to the brainstem.

Diencephalon

The diencephalon consists of the thalamus (main sensory relay center), the epithalamus (the pineal gland may play a role in sexual maturation), and the hypothalamus (important in maintaining homeostasis).

Cerebrum

The cerebrum has two hemispheres, each divided into lobes: the frontal, parietal, occipital, and temporal lobes.

8.9 Sensory Functions

1. The CNS constantly receives sensory input.
2. We are unaware of much of the input, but it is vital to our survival.
3. Some sensory input results in sensation.

Ascending Tracts

1. Ascending tracts transmit action potentials from the periphery to the brain.
2. Each tract carries a specific type of sensory information.

Sensory Areas of the Cerebral Cortex

1. Ascending tracts project to primary sensory areas of the cerebral cortex.
2. Association areas are involved in recognizing the sensory input.

8.10 Somatic Motor Functions

1. Somatic motor functions include involuntary and voluntary movements.
2. Upper motor neurons in the cerebral cortex connect to lower motor neurons in the spinal cord or cranial nerve nuclei.

Motor Areas of the Cerebral Cortex

1. Upper motor neurons are located in the primary motor cortex.
2. The premotor and prefrontal areas regulate movements.

Descending Tracts

Descending tracts project directly from upper motor neurons in the cerebral cortex to lower motor neurons in the spinal cord and brainstem; indirectly, they project from basal nuclei, the cerebellum, or the cerebral cortex through the brainstem to lower motor neurons in the spinal cord.

Basal Nuclei

1. Basal nuclei help plan, organize, and coordinate motor movements and posture.
2. People with basal nuclei disorders exhibit increased muscle tone and exaggerated, uncontrolled movements when at rest.

Cerebellum

1. The cerebellum is involved in balance, muscle tone, and muscle coordination.
2. Through its comparator function, the cerebellum compares the intended action to what is occurring and modifies the action to eliminate differences.
3. If the cerebellum is damaged, muscle tone decreases and fine motor movements become very clumsy.

8.11 Other Brain Functions

Communication Between the Right and Left Hemispheres

1. Each hemisphere controls the opposite half of the body.
2. Commissures connect the two hemispheres.
3. The left hemisphere is thought to be the dominant analytical hemisphere, and the right hemisphere is thought to be dominant for spatial perception and musical ability.

Speech

Speech involves the sensory speech area, the motor speech area, and the interactions between them and other cortical areas.

Brain Waves and Consciousness

An EEG monitors brain waves, which are a summation of the electrical activity of the brain.

Memory

1. The types of memory are working (lasting a few seconds to minutes), short-term (lasting a few minutes), and long-term (permanent) memory.
2. Long-term memory includes declarative and procedural memories.

Limbic System and Emotions

1. The limbic system includes the olfactory cortex, deep cortical regions, and nuclei.
2. The limbic system is involved with memory, motivation, mood, and other visceral functions. Olfactory stimulation is a major influence.

8.12 Meninges, Ventricles, and Cerebrospinal Fluid

Meninges

Three connective tissue meninges cover the CNS: the dura mater, arachnoid mater, and pia mater.

Ventricles

1. The brain and spinal cord contain fluid-filled cavities: the lateral ventricles in the cerebral hemispheres, a third ventricle in the diencephalon, a cerebral aqueduct in the midbrain, a fourth ventricle at the base of the cerebellum, and a central canal in the spinal cord.
2. The fourth ventricle has openings into the subarachnoid space.

Cerebrospinal Fluid

Cerebrospinal fluid is formed in the choroid plexuses in the ventricles. It exits through the fourth ventricle and reenters the blood through arachnoid granulations in the superior sagittal sinus.

8.13 Cranial Nerves

1. There are 12 pairs of cranial nerves: 3 with only sensory function (S), 4 with only somatic motor function (M), 1 with somatic motor (M) and sensory function (S), 1 with somatic motor and parasympathetic (P) function, and 3 with all three functions. Four of the cranial nerves have parasympathetic function.
2. The cranial nerves are olfactory (I; S), optic (II; S), oculomotor (III; M, P), trochlear (IV; M), trigeminal (V; S, M), abducens (VI; M), facial (VII; S, M, P), vestibulocochlear (VIII; S), glossopharyngeal (IX; S, M, P), vagus (X; S, M, P), accessory (XI; M), and hypoglossal (XII; M).

8.14 Autonomic Nervous System

1. The autonomic nervous system contains preganglionic and postganglionic neurons.
2. The autonomic nervous system has sympathetic and parasympathetic divisions.

Anatomy of the Sympathetic Division

1. Preganglionic cell bodies of the sympathetic division lie in the thoracic and upper lumbar regions of the spinal cord.
2. Postganglionic cell bodies are located in the sympathetic chain ganglia or in collateral ganglia.

Anatomy of the Parasympathetic Division

1. Preganglionic cell bodies of the parasympathetic division are associated with some of the cranial and sacral nerves.
2. Postganglionic cell bodies are located in terminal ganglia, either near or within target organs.

Autonomic Neurotransmitters

1. All autonomic preganglionic and parasympathetic postganglionic neurons secrete acetylcholine.
2. Most sympathetic postganglionic neurons secrete norepinephrine.

Functions of the Autonomic Nervous System

1. The sympathetic division prepares a person for action by increasing heart rate, blood pressure, respiration, and release of glucose for energy.

2. The parasympathetic division is involved in involuntary activities at rest, such as the digestion of food, defecation, and urination.

8.15 Enteric Nervous System

1. The enteric nervous system forms plexuses in the digestive tract wall.
2. Enteric neurons are sensory, motor, or interneurons; they receive CNS input but can also function independently.

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REMEMBERING AND UNDERSTANDING

1. List the functions of the nervous system.
2. Distinguish between the CNS and PNS.
3. Define the sensory and motor divisions of the PNS and the somatic and autonomic nervous systems.
4. What are the functions of neurons? Name the three parts of a neuron.
5. List the three types of neurons based on the organization of their processes.
6. Define glial cell. Name and describe the functions of the different glial cells.
7. What are the differences between unmyelinated and myelinated axons? Which conduct action potentials more rapidly? Why?
8. For nuclei, ganglia, nerve tracts, and nerves, name the cells or parts of cells found in each, state if they are white or gray matter, and name the part of the nervous system (CNS or PNS) in which they are found.
9. Explain the resting membrane potential and the roles of the K^+ leak channels and the sodium-potassium pump.
10. List the series of events at the membrane that generate an action potential, including the contributions of chemically gated and voltage-gated ion channels.

11. Describe the sequence of events at a synapse, starting with an action potential in the presynaptic neuron and ending with the generation of an action potential in the postsynaptic neuron.
12. Describe the primary function of neurotransmitters at the synapse.
13. Define a reflex. Name the five components of a reflex arc, and explain its operation.
14. Compare and contrast the two major types of neuronal pathways. Give an example of each.
15. Describe the importance of spatial and temporal summation.
16. Describe the spinal cord gray matter. Where are sensory and motor neurons located in the gray matter?
17. Differentiate between the ventral root and the dorsal root in relation to a spinal nerve. Which contains sensory fibers, and which contains motor fibers?
18. Describe the knee-jerk and withdrawal reflexes.
19. List the spinal nerves by name and number.
20. Name the three main plexuses and the major nerves derived from each.
21. Name the four parts of the brainstem, and describe the general functions of each.
22. Name the three main components of the diencephalon, describing their functions.
23. Name the four lobes of the cerebrum, and describe the location and function of each.
24. List the ascending tracts, and state their functions.
25. Describe the locations in the cerebral cortex of the primary sensory areas and their association areas. How do the association areas interact with the primary areas?
26. Distinguish between upper and lower motor neurons.
27. Distinguish among the functions of the primary motor cortex, premotor area, and prefrontal area.
28. List the descending tracts, and state their functions.
29. Describe the functions of the basal nuclei.
30. Describe the comparator activities of the cerebellum.
31. What are the differences in function between the right and left cerebral hemispheres?

32. Describe the process required to speak a word that is seen compared to one that is heard.
33. Name the three types of memory, and describe the processes that result in long-term memory.
34. What is the function of the limbic system?
35. Name and describe the three meninges that surround the CNS.
36. Describe the production and circulation of the cerebrospinal fluid. Through what structures does the cerebrospinal fluid return to the blood?
37. What are the three principal functional categories of the cranial nerves? List a specific function for each cranial nerve.
38. Define preganglionic neuron and postganglionic neuron.
39. Compare the structure of the somatic nervous system and the autonomic nervous system in terms of the number of neurons between the CNS and the effector organs and the types of effector organs.
40. Contrast the functions of the sympathetic and parasympathetic divisions of the autonomic nervous system.
41. What kinds of neurons (sympathetic or parasympathetic, preganglionic or postganglionic) are found in the following?
    a. cranial nerve nuclei
    b. lateral horn of the thoracic spinal cord gray matter
    c. lateral portion of the sacral spinal cord gray matter
    d. chain ganglia
    e. ganglia in the wall of an organ
42. List the three parts of the enteric nervous system.

CRITICAL THINKING

1. Given two series of neurons, explain why action potentials could be propagated along one series more rapidly than along the other series.

2. The left lung of a cancer patient was removed. To reduce the empty space left in the thorax after the lung was removed, the diaphragm on the left side was paralyzed so that the abdominal viscera would push the diaphragm upward into the space. What nerve should be cut to paralyze the left half of the diaphragm?
3. Name the nerve that, if damaged, produces the following symptoms:
   a. The elbow and wrist on one side are held in a flexed position and cannot be extended.
   b. The patient is unable to flex the right hip and extend the knee (as in kicking a ball).
4. A patient suffered brain damage in an automobile accident. Physicians suspected that the cerebellum was affected. On the basis of what you know about cerebellar function, how could you determine that the cerebellum was involved? What symptoms would you expect to see?
5. Landon was accidentally struck in the head with a baseball bat. He fell to the ground, unconscious. Later, when he had regained consciousness, he was unable to remember any of the events that happened during the 10 minutes before the accident. Explain.
6. Name the cranial nerve that, if damaged, produces the following symptoms:
   a. The patient is unable to move the tongue.
   b. The patient is unable to see out of one eye.
   c. The patient is unable to feel one side of the face.
   d. The patient is unable to move the facial muscles on one side.
   e. The pupil of one eye is dilated and does not constrict.
7. Why doesn't injury to the spinal cord at the level of C6 significantly interfere with nervous system control of the digestive system?

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

9

Senses

The senses include the general senses, such as touch and pain associated with the skin, as well as the special senses. The special senses include olfaction, taste, vision, hearing, and balance.

(photo): m-imagephotography/iStock/Getty Images

LEARN TO APPLY IT

Freddy is an older man but he has never needed glasses. He has several family members that are nearsighted, meaning they have problems seeing things at a distance, and require corrective lenses. Freddy, on the other hand, has had 20/20 vision his whole life. Lately, though, he has noticed that he can't see quite so well when he is reading. He jokes with his friends that his "arms seem to be getting shorter."

After reading about the process of vision, explain what type of vision problem Freddy is experiencing and how his joke about his arms getting shorter relates to his visual problem.

Answers to this question and the chapter's oddnumbered Apply It questions can be found in Appendix E.

Module 7 Nervous System

9.1 SENSATION

Learning Outcomes *After reading this section, you should be able to*

A. Define sensation.
B. Distinguish between general senses and special senses.

The **senses** are the means by which the brain receives information about the environment and the body. **Sensation** is the process initiated by stimulating sensory receptors, and **perception** is the conscious awareness of those stimuli. The brain constantly receives a wide variety of stimuli from both inside and outside the body, but stimulation of sensory receptors does not immediately result in perception. Sensory receptors respond to stimuli by generating action potentials that are propagated to the spinal cord and brain. Perception results when action potentials reach the cerebral cortex. Some other parts of the brain are also involved in perception. For example, the thalamus plays a role in the perception of pain.

Historically, five senses were recognized: smell, taste, vision, hearing, and touch. Today we recognize many more senses and divide them into two basic groups: general and special senses (figure. 9.1). The **general senses** have

receptors distributed over a large part of the body. They are divided into two groups: (1) the somatic senses and (2) the visceral senses. The **somatic senses** provide sensory information about the body and the environment. The **visceral senses** provide information about various internal organs, primarily involving pain and pressure.

Figure 9.1 **Classification of the Senses**

The senses are classified based on the location of the sensory receptors as well as the types of stimuli involved.

The receptors for the **special senses** are more specialized in structure and are localized to specific parts of the body. The special senses are (1) smell (olfaction), (2) taste, (3) vision, (4) hearing, and (5) balance.

9.2 SENSORY RECEPTORS

Learning Outcomes ***After reading this section, you should be able to***

A. List and describe five types of sensory receptors.

Sensory receptors are sensory nerve endings or specialized cells capable of responding to stimuli by developing action potentials. Several types of receptors are associated with both the general and the special senses, and each responds to a different type of stimulus:

Mechanoreceptors (MEK-an-noh-ree-SEP-ters) respond to mechanical stimuli, such as the bending or stretching of receptors.
Chemoreceptors (kee-moh-ree-SEP-ters) respond to chemicals. For example, odor molecules bind to chemoreceptors, allowing us to perceive smells.
Photoreceptors (foh-toh-ree-SEP-tors) respond to light.
Thermoreceptors (thur-moh-ree-SEP-ters) respond to temperature changes.
Nociceptors (NOH-see-sep-ters; *noceo,* to injure) respond to stimuli that result in the sensation of pain.

9.3 GENERAL SENSES

Learning Outcomes *After reading this section, you should be able to*

A. List the general senses and the receptor type associated with each.
B. Define and describe pain.
C. Define and describe referred pain.

The general senses have sensory receptors that are widely distributed throughout the body. The general senses include the senses of (1) touch, (2) pressure, (3) pain, (4) temperature, (5) vibration, (6) itch, and (7) **proprioception** (proh-pree-oh-SEP-shun), which is the sense of movement and position of the body and limbs.

Many of the receptors for the general senses are associated with the skin (figure 9.2); others are associated with deeper structures, such as tendons, ligaments, and muscles. Structurally, the simplest and most common types of sensory receptors are **free nerve endings.** These are relatively unspecialized neuronal branches similar to dendrites. Free nerve endings are distributed throughout almost all parts of the body. Some free nerve endings respond to painful stimuli, some to temperature, some to itch, and some to movement. Receptors for temperature are either **cold receptors** or **warm receptors.** Cold receptors respond to decreasing temperatures but stop responding at temperatures below 12°C (54°F). Warm receptors respond to increasing temperatures but stop responding at temperatures above 47°C (117°F). It is sometimes difficult to distinguish very cold from very warm objects touching the skin because only pain receptors are stimulated at temperatures below 12°C or above 47°C.

Figure 9.2 **Sensory Receptors in the Skin**

The sensory receptors of the skin vary in structure and sensitivity, allowing us to interact with our environment while still maintaining homeostasis.

Touch receptors are structurally more complex than free nerve endings. Many touch receptors are enclosed by capsules. There are several types of touch receptors (figure 9.2):

Merkel disks are small, superficial nerve endings involved in detecting light touch and superficial pressure.

Hair follicle receptors, associated with hairs, are also involved in detecting light touch. Light touch receptors are very sensitive but not very discriminative, meaning that the point being touched cannot be precisely located.

Meissner corpuscles are receptors for fine, discriminative touch and are located just deep to the epidermis. These receptors are very specific in localizing tactile sensations.

Ruffini corpuscles are deeper tactile receptors and play an important role in detecting continuous pressure in the skin.

Pacinian corpuscles are the deepest receptors and are associated with tendons and joints. These receptors relay information concerning deep pressure, vibration, and body position (proprioception).

Our sense of proprioception is important to our ability to maintain posture and to perform all the various body movements throughout our day. Proprioceptive information is conveyed not only to our cerebrum, where we have conscious awareness of our body position, but also to other areas of the brain, such as the cerebellum. This allows us to maintain posture and balance without constantly thinking about it. Interestingly, we have what is called a **righting reflex** that enables us to maintain an upright position, even if our body is on "uneven ground." If our body begins to lean to one side or the other, proprioceptors throughout the body, as well as balance receptors in the ear, detect this change. We adjust by moving our head to the normal upright position, and the muscles of our body adjust to allow the body to follow, thus restoring normal stance.

Pain

Pain is characterized by a group of unpleasant perceptual and emotional experiences. There are two types of pain sensation: (1) localized, sharp, pricking, or cutting pain resulting from rapidly conducted action potentials, and (2) diffuse, burning, or aching pain resulting from action potentials that are propagated more slowly.

Our perception of pain location differs depending on the types of receptors involved. Superficial pain sensations in the skin are highly localized as a result of the simultaneous stimulation of pain receptors and tactile receptors. Deep or visceral pain sensations are not highly localized because of the absence of tactile receptors in the deeper structures. Visceral pain stimuli are normally perceived as diffuse pain.

Perception of pain can be disrupted through anesthesia. **Local anesthesia** suppresses action potentials from pain receptors in local areas of the body through the injection of chemical anesthetics near a sensory receptor or nerve. Pain sensations can also be suppressed if loss of consciousness is produced. This is usually accomplished by **general anesthesia,** a treatment where chemical anesthetics that affect the reticular activating system are administered.

Pain sensations can also be influenced by inherent control systems. Sensory neurons associated with tactile receptors are linked to the pain sensory pathway in the CNS. Therefore, stimulation of these tactile receptors may inhibit pain perception. For example, rubbing the skin in the area of an injury often decreases the perception of pain. This may also explain why vigorous mental or physical activity decrease pain perception. Exercise programs are important components in the clinical management of chronic pain.

Referred Pain

Referred pain is perceived to originate in a region of the body that is not the source of the pain stimulus. Most commonly, we sense referred pain when deeper structures, such as internal organs, are damaged or inflamed (figure 9.3). This occurs because sensory neurons from the superficial area to which the pain is referred and the neurons from the deeper, visceral area where the pain stimulation originates converge onto the same ascending neurons in the spinal cord. The brain cannot distinguish between the two sources of pain stimuli, and the painful sensation is referred to the most superficial structures innervated, such as the skin.

Figure 9.3 **Areas of Referred Pain on the Body Surface**
Pain from the indicated internal organs is referred to the surface areas shown.

Referred pain is clinically useful in diagnosing the actual cause of the painful stimulus. For example, during a heart attack, pain receptors in the heart are stimulated when blood flow is blocked to some of the heart muscle. Heart attack victims, however, often may not feel the pain in the heart but

instead perceive cutaneous pain radiating from the left shoulder down the arm (figure 9.3).

Apply It 1

A man has constipation that causes distention and painful cramping in the colon (part of the large intestine). What kind of pain does he experience (localized or diffuse), and where does he perceive it? Explain.

9.4 SPECIAL SENSES

Learning Outcomes ***After reading this section, you should be able to***

A. List the special senses.

The senses of smell, taste, vision, hearing, and balance are associated with very specialized, localized sensory receptors. The sensations of smell and taste are closely related, both structurally and functionally, and both are initiated by the interaction of chemicals with chemoreceptors. The sense of vision is initiated by the interaction of light with photoreceptors. Both hearing and balance function in response to the interaction of mechanical stimuli with mechanoreceptors. Hearing occurs in response to sound waves, and balance occurs in response to gravity or motion.

9.5 OLFACTION

Learning Outcomes ***After reading this section, you should be able to***

A. Describe olfactory neurons, and explain how airborne molecules can stimulate action potentials in the olfactory nerves.

The sense of smell, called **olfaction** (ol-FAK-shun), occurs in response to airborne molecules, called **odorants,** that enter the nasal cavity. **Olfactory neurons** are bipolar neurons within the **olfactory epithelium,** which lines the superior part of the nasal cavity (figure 9.4*a*). The dendrites of the olfactory neurons extend to the epithelial surface, and their ends are modified with long, specialized cilia that lie in a thin mucous film on the epithelial surface. The mucus keeps the nasal epithelium moist, traps and dissolves airborne molecules, and facilitates the removal of molecules and particles from the nasal epithelium.

Figure 9.4 APR **Olfactory Epithelium and Olfactory Bulb**
(*a*) A sagittal section through the lateral wall of the nasal cavity shows the olfactory nerves, olfactory bulb, and olfactory tract. (*b*) The olfactory neurons lie within the olfactory epithelium. The axons of olfactory neurons pass through the cribriform plate to the olfactory bulb.

Airborne odorants become dissolved in the mucus on the surface of the epithelium and bind to receptor molecules on the membranes of the specialized cilia of the olfactory neurons. The binding of the odorant to the receptor initiates action potentials, which are then conducted to the olfactory cortex of the cerebrum by sensory neurons. There are at least 400 functional **olfactory receptors** in humans. Unlike most other receptors in the body,

each olfactory receptor can bind multiple types of odorants; conversely, each type of odorant can bind to multiple olfactory receptors. These multiple combinations of odorants and receptors allow us to detect an estimated 10,000 different smells. Once an odorant has bound to its receptor, that receptor is desensitized and does not respond to another odor molecule for some time, which helps with adaptation (described next) to a particular odor. The threshold for the detection of odors is extremely low, so very few odorants bound to an olfactory neuron can initiate an action potential. The olfactory range and sensitivity is even greater in some animals than in humans, due to a larger number and more types of olfactory receptors. For example, dogs are often used to detect small traces of explosives and other chemicals that people cannot detect.

Neuronal Pathways for Olfaction

The neuronal pathways of olfaction carry action potentials from the olfactory neurons to the areas of the cerebrum that allow for perception and interpretation of the stimuli. Axons from olfactory neurons form the olfactory nerves (cranial nerve I), which pass through foramina of the cribriform plate and enter the **olfactory bulb** (figure 9.4*b*). There the olfactory neurons synapse with interneurons that relay action potentials to the brain through the **olfactory tracts.** Each olfactory tract terminates in an area of the brain called the **olfactory cortex,** located within the temporal and frontal lobes. Olfaction is the only major sensation that is relayed directly to the cerebral cortex without first passing through the thalamus. This is a reflection of the older, more primitive origin of the olfactory cortex. The olfactory cortex is involved with both the conscious perception of smell and the visceral and emotional reactions that are often linked to odors.

Within the olfactory bulb and olfactory cortex are feedback loops that tend to inhibit transmission of action potentials resulting from prolonged exposure to a given odorant. This feedback, plus the temporary decreased sensitivity at the level of the receptors, results in **adaptation** to a given odor. For example, if you enter a room that has an odor, such as a movie theater that smells like popcorn, you adapt to the odor and cannot smell it as well after the first few minutes. If you leave the room for some time and then reenter the room, the odor again seems more intense.

9.6 TASTE

Learning Outcomes *After reading this section, you should be able to*

A. Outline the structure and function of a taste bud.

B. Describe the neuronal pathways for taste.

The sensory structures that detect taste stimuli are the **taste buds.** Taste buds are oval structures located on the surface of certain **papillae** (pah-PILL-ee; nipples), which are enlargements on the surface of the tongue (figure 9.5). Taste buds are also distributed throughout other areas of the mouth and pharynx, such as on the palate, the root of the tongue, and the epiglottis. Each taste bud consists of two types of cells. Specialized epithelial cells form the exterior supporting capsule of each taste bud, and the interior consists of about 40 **taste cells.** Each taste cell contains hairlike processes, called **taste hairs,** that extend through a tiny opening in the surrounding stratified epithelium, called a **taste pore.** Dissolved molecules or ions bind to receptors on the taste hairs and initiate action potentials, which sensory neurons carry to the insula of the cerebral cortex.

Figure 9.5 APR **Tongue**

(*a*) Dorsal surface of the tongue. (*b*) Section through a papilla showing the location of taste buds. (c) Enlarged view of a section through a taste bud.

Taste sensations are divided into five basic types: (1) sour, (2) salty, (3) bitter, (4) sweet, and (5) umami (oo-MAH-mee; savory). Although all taste buds are able to detect all five of the basic taste sensations, each taste bud is usually most sensitive to one class of taste stimuli. Presumably, our ability to perceive many different tastes is achieved through various combinations of these five basic types.

Heat damage to the tongue epithelial tissue can cause injury or even death to epithelial cells, including taste cells in the taste buds. If the epithelial cells are only damaged, taste sensation returns within a few hours to a few days. If the cells die, it takes about 2 weeks for the epithelial cells to be replaced.

Many taste sensations are strongly influenced by olfactory sensations. This influence can be demonstrated by comparing the taste of some food before and after pinching your nose. It is easy to detect that the sense of taste is reduced while the nose is pinched.

Neuronal Pathways for Taste

Taste sensations are carried to the brain by three cranial nerves: (1) the facial nerve, (2) the glossopharyngeal nerve, and (3) the vagus nerve (figure 9.6). The facial nerve (VII) transmits taste sensations from the anterior two-thirds of the tongue. The glossopharyngeal nerve (IX) carries taste sensations from the posterior one-third. The vagus nerve (X) carries some taste sensations from the root of the tongue. Axons from these three cranial nerves synapse in the gustatory (taste) portion of brainstem nuclei. Axons of neurons in these brainstem nuclei extend to and synapse with interneurons in the thalamus. Axons from neurons in the thalamus project to the taste area in the insula of the cerebrum (see figure 9.6).

Figure 9.6 **Pathways for the Sense of Taste**

The facial nerve (anterior two-thirds of the tongue), glossopharyngeal nerve (posterior one-third of the tongue), and vagus nerve (root of the tongue) all carry taste sensations. The trigeminal nerve carries tactile sensations from the anterior two-thirds of the tongue. The chorda tympani from the facial nerve (carrying taste input) joins the trigeminal nerve.

Understand ***Apply It 2***

Why doesn't food taste as good when you have a cold?

9.7 VISION

Learning Outcomes ***After reading this section, you should be able to***

A. List the accessory structures of the eye, and explain their functions.
B. Name the tunics of the eye, listing the parts of each tunic.
C. Describe the functions of each of the tunics of the eye.
D. Explain the differences in function between rods and cones.
E. Describe the chambers of the eye and the fluids they contain.
F. Describe the generation of action potentials at the retina.

G. Explain how images are focused on the retina.
H. Describe the visual pathways.

The visual system includes the eyes, the accessory structures, and sensory neurons. The eyes are housed within bony cavities called orbits. We obtain much of our information about the world through the visual system. For example, education is largely based on visual input and depends on our ability to read words and numbers. Visual input includes information about light and dark, movement and color. Visual input begins as action potentials originating in the eyes. These action potentials move along the visual pathways and convey visual information to the brain.

Accessory Structures of the Eye

Accessory structures protect, lubricate, and move the eye. They include the eyebrows, eyelids, conjunctiva, lacrimal apparatus, and extrinsic eye muscles (figures 9.7 and 9.8).

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Figure 9.7 APR **The Eye and Its Accessory Structures**
(*a*) Photo of left eye. (*b*) Sagittal section through the eye. (*c*) Lacrimal apparatus.
© Eric Wise

Figure 9.8 APR **Extrinsic Eye Muscles**

Extrinsic muscles of the right eye as seen from a lateral view with the lateral wall of the orbit removed. The medial rectus muscle cannot be seen from this view.

Eyebrows

The **eyebrows** protect the eyes by preventing perspiration from running down the forehead and into the eyes, causing irritation. They also help shade the eyes from direct sunlight (figure 9.7*a*).

Eyelids

The **eyelids,** with their associated lashes, protect the eyes from foreign objects (figure 9.7*a*,*b*). If an object suddenly approaches the eye, the eyelids protect the eye by closing and then opening quite rapidly (blink reflex). Blinking, which normally occurs about 20 times per minute, also helps keep the eyes lubricated by spreading tears over the surface.

Conjunctiva

The **conjunctiva** (kon-junk-TIE-vah) is a thin, transparent mucous membrane covering the inner surface of the eyelids and the anterior surface of the eye (figure 9.7*b*). The secretions of the conjunctiva help lubricate the surface of the eye. Conjunctivitis is an inflammation of the conjunctiva (see table 9.1, Representative Diseases and Disorders, at the end of this chapter).

Lacrimal Apparatus

The **lacrimal** (LAK-rim-al; tear) **apparatus** consists of a lacrimal gland situated in the superior lateral corner of the orbit and a nasolacrimal duct and

associated structures in the inferior medial corner of the orbit (figure 9.7*c*). The **lacrimal gland** produces a fluid we call tears, which pass over the anterior surface of the eye. Most of the fluid produced by the lacrimal glands evaporates from the surface of the eye, but excess tears are collected in the medial angle of the eyes by small ducts called **lacrimal canaliculi** (kan-ah-LIK-you-lie; little canals). These canaliculi open into a **lacrimal sac,** an enlargement of the **nasolacrimal** (NAY-zoh-LAK-rim-al) **duct.** Tears pass through the nasolacrimal duct into the nasal cavity. Tears lubricate and cleanse the eye. They also contain an enzyme that helps combat eye infections.

Apply It 3

Explain why it is often possible to smell (or "taste") medications, such as eyedrops, that have been placed into the eyes.

Extrinsic Eye Muscles

Each eyeball has six **extrinsic eye muscles** attached to its surface. These extrinsic muscles are skeletal muscles and are responsible for the movement of each eyeball (figure 9.8). Four of these muscles run more or less straight from their origins in the posterior portion of the orbit to their insertion sites on the eye, to attach to the four quadrants of the eyeball. They are the superior, inferior, medial, and lateral **rectus muscles.** Two muscles, the superior and inferior **oblique muscles,** are located at an angle to the long axis of the eyeball.

Anatomy of the Eye

The eyeball is a hollow, fluid-filled sphere. The wall of the eyeball is composed of three tissue layers, or **tunics** (figure 9.9).

Figure 9.9 APR **Sagittal Section of the Eye, Demonstrating Its Tunics**

The wall of the eyeball consists of three tunics, each of which is composed of specific components. The fibrous tunic includes the sclera and cornea. The vascular tunic includes the choroid, ciliary body, and iris. The nervous tunic consists of the retina.

1. The outer, **fibrous tunic** consists of the sclera and cornea.
2. The middle, **vascular tunic** consists of the choroid, ciliary body, and iris.
3. The inner **nervous tunic** consists of the retina.

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CLINICAL IMPACT

Corneal Transplants

The cornea was one of the first organs to be successfully transplanted. Corneal transplants are often performed when corneal damage due to injury or infection has severely altered the surface of the cornea. Several characteristics make it relatively easy to transplant: It is easily accessible and relatively easily removed from the donor and grafted to the recipient; it does not have blood vessels and therefore does not require the growth of extensive circulation into the tissue after grafting; and it is less

likely to stimulate the immune system and therefore less likely to be rejected than are other tissues.

Fibrous Tunic

The **sclera** (SKLAIR-ah; hard) is the firm, white, outer connective tissue layer of the posterior five-sixths of the fibrous tunic. The sclera helps maintain the shape of the eye, protects the internal structures, and provides attachment sites for the extrinsic eye muscles. A small portion of the sclera can be seen as the "white of the eye."

The **cornea** (KOR-nee-ah) is the transparent anterior sixth of the eye, which permits light to enter. As part of the focusing system of the eye, the cornea also bends, or refracts, the entering light.

Vascular Tunic

The middle tunic of the eye is called the **vascular tunic** because it contains most of the blood vessels of the eye. The posterior portion of the vascular tunic, associated with the sclera, is the **choroid** (KOR-oid). This very thin structure consists of a vascular network and many melanin-containing pigment cells, causing it to appear black. The black color absorbs light, so that it is not reflected inside the eye. If light were reflected inside the eye, the reflection would interfere with vision.

Anteriorly, the vascular tunic consists of the ciliary body and the iris. The **ciliary** (SILL-ee-air-ee) **body** is continuous with the anterior margin of the choroid. The ciliary body contains smooth muscles called **ciliary muscles,** which attach to the perimeter of the lens by **suspensory ligaments** (figure 9.10*a,b*). The **lens** is a flexible, biconvex, transparent disc (see figure 9.9 and figure 9.10*a*).

Figure 9.10 **Iris**

(*a*) Section of eyeball highlighting the ciliary body, as well as the chambers of the eye. (*b*) Contraction and relaxation of the ciliary muscles adjust the tension in the suspensory ligaments, which are attached to the lens. Alterations in the tension in the suspensory ligaments changes the shape of the lens. (*c*) Circular smooth muscles of the iris constrict the pupil. Radial smooth muscles of the iris dilate the pupil.

The **iris** is the colored part of the eye. It is attached to the anterior margin of the ciliary body, anterior to the lens. The iris is a contractile structure consisting mainly of smooth muscle surrounding an opening called the **pupil.** Light passes through the pupil, and the iris regulates the diameter of the pupil, which controls the amount of light entering the eye. Parasympathetic stimulation from the oculomotor nerve (III) causes the

circular smooth muscles of the iris to contract, constricting the pupil, whereas sympathetic stimulation causes radial smooth muscles of the iris to contract, dilating the pupil (figure 9.10*c*). As light intensity increases, the pupil constricts; as light intensity decreases, the pupil dilates.

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Nervous Tunic

The nervous tunic is the innermost tunic and consists of the **retina.** The retina covers the posterior five-sixths of the eye and is composed of two layers: (1) an outer **pigmented retina** and (2) an inner **sensory retina** (figure 9.11). The pigmented retina, with the choroid, keeps light from reflecting back into the eye. The sensory retina contains photoreceptor cells as well as numerous interneurons (figure 9.11).

Figure 9.11 APR **Retina**

Enlarged section through the retina, with its major layers labeled.

Photoreceptor cells, which include **rods** and **cones,** respond to light. Over most of the retina, rods are 20 times more common than cones. Rods can function in dim light because they are very sensitive, meaning they require lower levels of light to be stimulated. Rods, however, do not provide color vision. Cones require much more light, and they do provide color vision. There are three types of cones, each sensitive to a different color: blue, green, or red. The interneurons of the sensory retina, some of which are identified in figure 9.11, regulate and relay changes in photoreceptor activity along the visual pathway.

Apply It 4

In dim light, colors seem to fade and objects appear in shades of gray. Explain this phenomenon.

When the posterior region of the retina is examined with an ophthalmoscope (of-THAL-moh-scope), two major features can be observed: (1) the macula and (2) the optic disc (figure 9.12*a*). The **macula** (MAK-you-lah) is a small spot near the center of the posterior retina. In the center of the macula is a small pit, the **fovea** (FOH-vee-ah; pit) **centralis.** The fovea centralis is the part of the retina where light is most focused when the eye is looking directly at an object. The fovea centralis contains only cone cells, and the cells are more tightly packed there than anywhere else in the retina. Hence, the fovea centralis is the region with the greatest ability to discriminate fine images, which explains why objects are best seen straight ahead.

Figure 9.12 APR **Ophthalmoscopic View of the Retina**

(*a*) This view shows the posterior wall of the left eye as seen through the pupil. Notice the vessels entering the eye through the optic disc. The macula, with the fovea centralis in the center, is located lateral to the optic disc. (*b*) Demonstration of the blind spot. Close your right eye. Hold the drawing in front of your left eye and stare at the +. Move the drawing toward your eye. At a certain point, when the image of the spot is over the optic disc, the red spot seems to disappear.

(*a*) Steve Allen/Getty Images RF

The **optic disc** is a white spot just medial to the macula, through which a number of blood vessels enter the eye and spread over the surface of the retina. This is also the spot at which axons from the retina meet, pass through the two outer tunics, and exit the eye as the optic nerve. The optic disc contains no photoreceptor cells and does not respond to light; it is therefore called the **blind spot** of the eye. A small image projected onto the blind spot cannot be seen (figure 9.12*b*).

Chambers of the Eye

The interior of the eyeball is divided into three areas, or chambers: (1) the **anterior chamber,** (2) **the posterior chamber,** and (3) the **vitreous** (VIT-ree-us; glassy) **chamber** (see figure 9.9). The anterior and posterior chambers are located between the cornea and the lens. The iris separates the

anterior and the posterior chambers, which are continuous with each other through the pupil. The much larger vitreous chamber is posterior to the lens.

The anterior and posterior chambers are filled with **aqueous humor** (watery fluid), which helps maintain pressure within the eye, refracts light, and provides nutrients to the inner surface of the eye. Aqueous humor is produced by the ciliary body as a blood filtrate and is returned to the blood through a venous ring that surrounds the cornea. The presence of aqueous humor keeps the eye inflated, much like the air in a basketball. If aqueous humor flow from the eye through the venous ring is blocked, the pressure in the eye increases, resulting in a condition called **glaucoma** (see table 9.1, Representative Diseases and Disorders near the end of this chapter). Glaucoma can eventually lead to blindness because the fluid compresses the retina, thereby restricting blood flow through it.

The vitreous chamber of the eye is filled with a transparent, jellylike substance called **vitreous humor** (see figure 9.9). The vitreous humor helps maintain pressure within the eye and holds the lens and the retina in place. It also refracts light. Unlike the aqueous humor, the vitreous humor does not circulate.

Functions of the Eye

The eye functions much like a camera. Images are perceived based on light passing into the eye and altering the activity of the photoreceptors in the retina. Just like with a camera, the clarity of the image is determined by the eye's ability to focus the light. Figure 9.13 illustrates the basic processes involved in vision:

1. The pupil allows light into the eye, which is focused by the cornea, lens, and humors onto the retina.
2. The light striking the photoreceptors of the retina produces action potentials within the visual pathway.
3. The optic nerve conveys these action potentials to the brain where perception occurs.

PROCESS Figure

PROCESS Figure 9.13 **The Process of Vision**

The process of vision involves the stimulation of photoreceptors as light is focused on the retina.

Considering the steps outlined in the figure, which steps would involve the movement of ions across cell membranes. Explain your answer.

Light Refraction

An important characteristic of light is that it can be refracted (bent). As light passes from air to some other, denser transparent substance, the light rays are refracted. If the surface of a lens is concave, the light rays are bent, so that they diverge as they pass through the lens. If the surface is convex, like the outer surface of the cornea (see figure 9.9), the light rays converge. As the light rays converge, they finally reach a point at which they cross. The crossing point is called the **focal point (FP)** (figure 9.14), and causing light to converge is called **focusing.** The focal point in the eye occurs just anterior to the retina, and the tiny image that is focused on the retina is inverted compared to the actual object.

Figure 9.14 **Focus by the Eye**

The focal point (FP) is where light rays cross. (*a*) When viewing a distant image, the lens is flattened, and the image is focused on the retina. (*b*) In accommodation for near vision, the lens becomes more rounded, allowing the image to be focused on the retina.

Focusing Images on the Retina

The cornea is a convex structure, and as light rays pass from the air through the cornea, they converge (figure 9.14). Additional convergence occurs as light passes through the aqueous humor, lens, and vitreous humor. The greatest contrast in media density is between the air and the cornea. The greatest amount of convergence therefore occurs at that point. However, the shape of the cornea and its distance from the retina are fixed, so the cornea cannot make any adjustment in focus. Fine adjustments in focus are accomplished by changing the shape of the lens.

The ciliary muscles contract and relax, changing the tension in the suspensory ligaments. However, the changes in tension are not as straightforward as one would think. When the ciliary muscles are relaxed, the tension in the suspensory ligaments is high and the suspensory ligaments maintain elastic pressure on the perimeter of the lens. This pressure keeps the lens relatively flat and allows for distant vision (figure 9.14*a*). When an object is brought closer than 20 feet (about 6½ m) from the eye, the ciliary muscles contract as a result of parasympathetic stimulation, pulling the ciliary body toward the lens. The movement of the ciliary body toward the lens reduces the tension in the suspensory ligaments of the lens. The lens will then assume a more spherical form because of its own internal elastic nature (figure 9.14*b*). The spherical lens has a more convex surface, causing greater refraction of light. This process of changing the shape of the lens is called

accommodation and it enables the eye to focus on images closer than 20 feet from the eye.

Apply It 5

As you are driving a car, what changes occur when you look down at the speedometer and then back up at the road?

When a person's vision is tested, a chart is placed 20 feet from the eye, and the person is asked to read a line of letters that has been standardized for normal vision. If the person can read the line, he or she has 20/20 vision, which means that the person can see at 20 feet what people with normal vision see at 20 feet. On the other hand, if the person can only read at 20 feet the line that people with normal vision see at 40 feet, the person's eyesight is 20/40, and corrective lenses are probably needed.

As we age, the lenses of the eyes lose flexibility (see Effects of Aging on Senses, later in the chapter). The ability for the lenses to change shape is diminished, leading to a vision impairment. (Note: This information is helpful for answering the Learn to Apply It question at the beginning of the chapter.)

Action Potential Generation at the Retina

As stated earlier, photoreceptors in the retina respond to light, allowing for the process of vision. Photoreceptors are specialized cells. The outer segments of photoreceptors are modified by numerous foldings of the cell membrane to form discs (figure 9.15*a-c*). Rod photoreceptors contain a photosensitive pigment called **rhodopsin** (roh-DOP-sin; purple pigment). Rhodopsin consists of a protein **opsin** (OP-sin) loosely bound to a yellow pigment called **retinal** (RET-ih-nal) (figure 9.15*d*). It is the interaction between light and photosensitive pigments, such as rhodopsin, that result in action potentials in the retina. Figure 9.16 illustrates the effect of light on rhodopsin.

❶ Prior to light exposure, a rhodopsin molecule is intact, with the opsin and retinal combined.

❷ When exposed to light, retinal changes shape, which then changes the activity of the entire rhodopsin molecule.

❸ This change in rhodopsin stimulates a response in the rods, resulting in vision.

❹ Retinal then completely detaches from opsin.

❺ Energy (ATP) is required to change retinal back to its original form.

❻ The change in form allows retinal to reattach to opsin and return rhodopsin to the form it had before it was stimulated by light.

Figure 9.15 **Photoreceptors**

(*a*) Rod cell. (*b*) Cone cell. (*c*) Enlargement of the discs in the outer segment. (*d*) Enlargement of one of the discs, showing the relationship of rhodopsin to the membrane.

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PROCESS Figure

PROCESS Figure 9.16 **Effect of Light on Rhodopsin**

When exposed to light, rhodopsin is activated as retinal changes shape and detaches from opsin. ATP is needed to recombine the opsin and retinal.

A common symptom of mitochondrial diseases is blindness. Recall from chapter 3 that mitochondria are the major sites of ATP production. Based on what you have learned about the function of rhodopsin, state a hypothesis that might explain the relationship between mitochondrial disease and blindness.

CLINICAL IMPACT

Color Blindness

Color blindness is the absence of perception of one or more of perception of one or more color Figure 9.17). Recall that color perception is the result of activation of different populations of cones. Color perception may be decreased or completely lost. The loss may involve perception of all three colors or of one or two colors. Most forms of color blindness occur more frequently in males and are X-linked genetic traits (see chapter 20). In Western Europe, about 8% of all males have some form of color blindness, whereas only about 1% of the females are color blind.

Figure 9.17 These color blindness charts demonstrate the differences in color perception associated with some forms of color blindness. (*a*) A person with normal vision can see the number 74, whereas a person with red-green color blindness sees the number 21. (*b*) A person with normal vision can see the number 5. A person with red-green color blindness sees the number 2.

(a) Steve Allen/Getty Images; (b) Prisma Bildagentur AG/Alamy Stock Photo

Reproduced from *Ishihara's Tests for Colour Deficiency* published by Kanehara Trading, Inc., Tokyo, Japan. Tests for color deficiency cannot be conducted with this material. For accurate testing, the original plates should be used.

The manufacture of retinal in rods takes time and requires vitamin A. In bright light, much of the rhodopsin in rods is dissociated (opsin and retinal are separated). For example, suppose you go into a dark building on a bright day. It will take several seconds for your eyes to adjust to the dark as opsin and retinal reassociate to form rhodopsin in the rods, which can then react to

the dim light. A person with a vitamin A deficiency may have a condition called **night blindness,** characterized by difficulty seeing in dim light. Night blindness can also result from **retinal detachment,** which is the separation of the sensory retina from the pigmented retina. Retinal detachment affects the periphery of the retina, where the rods are located, more than the center of the retina, where the cones are located. Because the rods are more sensitive than the cones to light, retinal detachment affects vision in low light to a greater extent than vision in bright light.

The photosensitive pigments in cone cells are slightly different from those in rod cells. The pigments in cone cells allow for the perception of colors. Each color is associated with a certain wavelength of light. Three major types of color-sensitive opsin exist; they are sensitive to blue, red, or green. The many colors that we can see result from the stimulation of combinations of these three types of cones.

As stated earlier in this section, the sensory retina also contains interneurons, including bipolar cells, horizontal cells, and ganglion cells. The rod and cone cells synapse with bipolar cells of the sensory retina (see figure 9.11). These and the horizontal cells of the retina modify the output of the rod and cone cells. For example, this modification helps us perceive the borders between objects of contrasting brightness. The bipolar and horizontal cells synapse with ganglion cells, whose axons converge at the posterior of the eye to form the **optic nerve** (II; see figures 9.9 and 9.11).

Neuronal Pathways for Vision

Figure 9.18 shows the neuronal pathways that transmit signals generated by light from the time light enters the eye until it reaches the area of the brain where vision is perceived.

❶ Each eye has an area from which it collects light. This area is referred to as the visual field. Each field is divided into the temporal part and the nasal part.

❷ After passing through the cornea and lens, light from each half of the visual field projects to the opposite side of the retina, stimulating photoreceptors. Action potentials are conducted along the optic nerve.

❸ The **optic nerve** leaves the eye and exits the orbit through the optic foramen to enter the cranial cavity. Just inside the cranial cavity, the two optic nerves connect to each other at the **optic chiasm** (KAI-azm; crossing). Though it may appear that all the fibers of the optic nerves cross over and extend to the opposite side of the brain, that is not completely accurate. Each side of the brain receives signals from each eye.

Axons from the nasal (medial) part of each retina cross through the optic chiasm and project to the opposite side of the brain. Axons from the temporal (lateral) part of each retina pass through the optic nerves and project to the brain on the same side of the body without crossing.

4. Beyond the optic chiasm, the route of the ganglionic axons is through the two optic tracts. Most of the **optic tract** axons terminate in the thalamus
5. Neurons from the thalamus form the fibers of the **optic radiations,** which project to the **visual cortex** in the occipital lobe of the cerebrum. The visual cortex is the area of the cerebrum where vision is perceived.
6. The right part of each visual field projects to the left side of the brain, and the left side of each visual field projects to the right side of the brain.

PROCESS Figure

PROCESS Figure 9.18 APR **Visual Pathways**

Pathways for both eyes *(superior view)*.

Predict the effects of a lesion occurring in the left optic nerve just anterior to the optic chiasm. How would this differ if the lesion occurred on the left side of the visual pathway posterior to the optic chiasm?

The image seen by each eye is the **visual field** of that eye (figure 9.18). Depth perception (three-dimensional, or binocular, vision) requires both eyes and occurs where the two visual fields overlap (figure 9.19). Each eye sees a slightly different (monocular) view of the same object. The brain then processes the two images into a three-dimensional view of the object. If only one eye is functioning, the view of the object is flat, much like viewing a photograph.

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Figure 9.19 **Binocular Vision**

Overlap of the fields of vision (superior view).

The most common cause of **diplopia,** or double vision, is misalignment of the two eyes (binocular diplopia). This often results from weakness of the muscles moving the eyes. Most adults cannot easily ignore the double image and may need to wear a patch over one eye to eliminate one image. In children with diplopia, the brain may compensate for the two discordant

images by ignoring one of the images; thus, the problem appears to go away. Double vision should not be ignored, because it can be a symptom of a serious neurological problem, such as an expanding brain tumor compressing the nerves to the eye muscles and decreasing their function. A physician should be consulted as soon as possible.

9.8 HEARING AND BALANCE

Learning Outcomes *After reading this section, you should be able to*

A. Describe the structures of the outer ear, and state the function of each.
B. Describe the structures of the middle ear, and state the function of each.
C. Describe the anatomy of the cochlea, and explain how sounds are detected.
D. Explain how the structures of the vestibule and semicircular canals function in static and dynamic equilibrium.

The organs of hearing and balance are located in the ears. Each ear is divided into three areas: (1) the external ear, (2) the middle ear, and (3) the inner ear (figure 9.20). The **external ear** is the part extending from the outside of the head to the tympanic membrane, commonly called the eardrum. The **middle ear** is an air-filled chamber medial to the tympanic membrane. The **inner ear** is a set of fluid-filled chambers medial to the middle ear. The external and middle ears conduct sound waves toward the inner ear and are involved in hearing only, whereas the inner ear functions in both hearing and balance.

Figure 9.20 APR **Structure of the Ear**

A medial view of the three regions of the ear: the external ear, the middle ear, and the inner ear.

Anatomy and Function of the Ear

External Ear

The **auricle** (AW-ri-kul) is the fleshy part of the external ear on the outside of the head. The auricle opens into the **external auditory canal,** a passageway that leads to the eardrum. The auricle collects sound waves and directs them toward the external auditory canal, which transmits them to the tympanic membrane. The skin that lines the auditory canal has both hairs and **ceruminous** (se-ROO-mi-nus; *cera,* wax) **glands.** The ceruminous glands produce **cerumen** (seh-ROO-men), a modified sebum commonly called earwax. The hairs and cerumen help prevent foreign objects from reaching the delicate tympanic membrane.

The **tympanic** (tim-PAN-ik; drumlike) **membrane,** or *eardrum,* is a thin membrane that separates the external ear from the middle ear. It consists of a thin layer of connective tissue sandwiched between two epithelial layers. Sound waves reaching the tympanic membrane cause it to vibrate.

Middle Ear

Medial to the tympanic membrane is the air-filled cavity of the middle ear. Two covered openings on the medial side of the middle ear, the **oval window** and the **round window,** connect the middle ear with the inner ear. The middle ear contains three **auditory ossicles** (OS-ik-elz; ear bones): (1) the **malleus** (MAL-ee-us; hammer), (2) the **incus** (IN-cuss; anvil), and (3) the **stapes** (STAY-pees; stirrup). The auditory ossicles form a flexible, bony bridge that transmits vibrations from the tympanic membrane to the oval window. The malleus is attached to the medial surface of the tympanic membrane. The incus connects the malleus to the stapes. The base of the stapes is seated in the oval window, surrounded by a flexible ligament. As vibrations are transmitted from the malleus to the stapes, the force of the vibrations is amplified about 20-fold because the area of the tympanic membrane is about 20 times that of the oval window. Two small muscles in the middle ear, one attached to the malleus and the other to the stapes, help dampen vibrations caused by loud noises, thus protecting the delicate inner ear structures.

There are two unblocked openings into the middle ear. One opens into the mastoid air cells in the mastoid process of the temporal bone. The other, called the **auditory tube,** or *eustachian* (you-STAY-shun) *tube*, opens into the pharynx and enables air pressure to be equalized between the outside air and the middle ear cavity. Unequal pressure between the middle ear and the outside environment can distort the tympanic membrane, dampen its vibrations, and make hearing difficult. Distortion of the tympanic membrane also stimulates pain receptors associated with that structure. That distortion is why, as a person changes altitude, sounds seem muffled and the person may experience ear pain. These symptoms can be relieved by opening the auditory tube to allow air to enter or exit the middle ear, such as by swallowing, yawning, chewing, or holding the nose and mouth shut while gently forcing air out of the lungs.

Inner Ear

The inner ear consists of interconnecting tunnels and chambers within the temporal bone, called the **bony labyrinth** (LAB-ih-rinth; maze) (figure 9.21*a*). Inside the bony labyrinth is a smaller set of membranous tunnels and

chambers called the **membranous labyrinth** (figure 9.21*b*). The membranous labyrinth is filled with a clear fluid called **endolymph** (EN-doh-limf), and the space between the membranous and bony labyrinths is filled with a fluid called **perilymph** (PER-i-limf). The bony labyrinth can be divided into three regions: (1) the cochlea, (2) the vestibule, and (3) the semicircular canals. The cochlea is involved in hearing. The vestibule and semicircular canals are involved primarily in balance.

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Figure 9.21 APR **Structure of the Inner Ear**

(*a*) Bony labyrinth. The outer surface is the periosteum lining the inner surface of the bony labyrinth. (*b*) In this cross section of the cochlea, the outer layer is the periosteum lining the inner surface of the bony labyrinth. The membranous labyrinth is very small in the cochlea and consists of the vestibular and basilar membranes. The space between the membranous and bony labyrinths consists of two parallel tunnels: the scala vestibuli and the scala tympani. (*c*) An enlarged section of the cochlear duct (membranous labyrinth). (*d*) A greatly enlarged individual sensory hair cell. (*e*) Scanning electron micrograph of the microvilli of a hair cell.

(e) Courtesy of A. J. Hudspeth

The **cochlea** (KOK-lee-ah; snail shell) is shaped like a snail shell (figure 9.21*a*) and contains a bony core shaped like a screw. The threads of this screw are called the **spiral lamina.** The cochlea is divided into three channels: (1) the scala vestibuli, (2) the scala tympani, and (3) the cochlear duct (figure 9.21*b*). The **scala vestibuli** (SKA-lah ves-TIB-you-lie; *scala,* stairway) extends from the oval window to the apex of the cochlea. The **scala tympani** (tim-PA-nee) extends in parallel with the scala vestibuli from the apex back to the round window. These two channels are perilymph-filled spaces between the walls of the bony and membranous labyrinths. The wall of the membranous labyrinth that lines the scala vestibuli is called the **vestibular** (ves-TIB-you-lar) **membrane;** the wall of the membranous labyrinth that lines the scala tympani is the **basilar membrane.** The **cochlear duct** is formed by the space between the vestibular membrane and the basilar membrane and is filled with endolymph.

Inside the cochlear duct is a specialized structure called the **spiral organ,** or *organ of Corti* (figure 9.21*c*). The spiral organ contains specialized sensory cells called **hair cells,** which have hairlike microvilli, often referred to as stereocilia, on their surfaces (figure 9.21*c*,*d*,*e*). The microvilli are stiffened by actin filaments. The hair tips are embedded within an acellular gelatinous shelf called the **tectorial** (tek-TOR-ee-al; a covering) **membrane,** which is attached to the spiral lamina (figure 9.21*b*,*c*).

Hair cells have no axons of their own, but each hair cell is associated with axon terminals of sensory neurons, the cell bodies of which are located within the **cochlear ganglion,** or *spiral ganglion*. Axons of the sensory neurons join to form the cochlear nerve. This nerve joins the vestibular nerve to become the **vestibulocochlear nerve** (VIII), which carries action potentials to the brain.

Hearing

The process of hearing involves two major steps: (1) conduction of sound waves and (2) stimulation of hearing receptors. Conduction involves structures of the outer, middle, and inner ears. Stimulation of hearing

receptors occurs in the inner ear. Figure 9.22 illustrates the process of hearing.

PROCESS Figure

PROCESS Figure 9.22 APR **Effect of Sound Waves on Middle and Inner Ear Structures**

Effect of Sound Waves on Middle and Inner Ear Structures

Sound waves in the air are conducted through the ear until they stimulate hair cells in the spiral organ.

Explain why fluid accumulation in the middle ear would reduce a person's ability to hear.

❶ Vibrations create sound waves. Sound waves are collected by the auricle and conducted through the external auditory canal toward the tympanic membrane. Sound waves strike the tympanic membrane and cause it to vibrate.

❷ Movement of the tympanic membrane causes vibration of the three ossicles of the middle ear. The auditory ossicles form a “bony bridge”

conducting and amplifying the vibration from the tympanic membrane to the oval window.

❸ Vibrations of the base of the stapes, seated in the oval window, produce waves in the perilymph of the cochlea. The two scalae can be thought of as a continuous, U-shaped tube, with the oval window at one end of the scala vestibuli and the round window at the other end of the scala tympani. The vibrations of the stapes in the oval window cause movement of the perilymph. The perilymph moves as a wave through the scala vestibuli to the scala tympani, finally pushing against the membrane covering the round window.

❹ The flexibility of the membrane allows the perilymph to move.

❺ The waves produced in the perilymph pass through the vestibular membrane and cause vibrations of the endolymph. Waves in the endolymph, within the cochlear duct, cause displacement of the basilar membrane.

❻ As the basilar membrane is displaced, the hair cells, seated on the basilar membrane, move with the membrane. The microvilli of the hair cells are embedded in the tectorial membrane, which is a rigid shelf that does not move. Because one end of the microvilli moves with the hair cells and their other ends are embedded in the nonmoving tectorial membrane, the microvilli bend. The bending of the microvilli stimulates the hair cells, which induces action potentials in the cochlear nerves.

❼ As described in step 4, vibrations in the perilymph continue to move through the scala tympani toward the round window, where they are dampened.

Understand

Apply It 6

When you hear a faint sound, why do you turn your head toward it?

Sound is a result of vibration. When describing these vibrations, we refer to them as sound waves. Sounds are often described relative to their pitch and volume. **Pitch** is the frequency, or wavelength, of sound. **Volume** is related to the amplitude of the sound wave.

The width and structure of the basilar membrane are not uniform throughout its length. The membrane is narrower and denser near the oval window and wider and less dense near the tip of the cochlea. The various regions of the membrane can be compared to the strings in a piano (i.e., some

are short and thick, and others are longer and thinner). As a result of this organization, sounds with higher **pitches (shorter wavelengths)** cause maximum distortion of the basilar membrane nearer the oval window, whereas sounds with lower pitches (longer wavelengths) cause maximum distortion nearer the apex of the cochlea. In each case, different hair cells are stimulated, and because of the differences in which hair cells are maximally stimulated, a person is able to detect variations in pitch. In relation to volume, louder sounds have higher wave amplitudes and cause the basilar membrane to distort more intensely. As a result, the hair cells are stimulated more often, generating more action potentials along the auditory pathway.

Hearing impairment can have many causes. In general, there are two categories of hearing impairment: (1) conduction deafness and (2) sensorineural hearing loss (see table 9.1 at the end of this chapter). **Conduction deafness** results from mechanical deficiencies— for example, destruction of the ligament that holds the malleus and incus together. **Sensorineural hearing loss** is caused by deficiencies in the spiral organ or nerves; for example, loud sounds can damage the delicate microvilli of the hair cells, leading to destruction of the spiral organ.

Neuronal Pathways for Hearing

The senses of hearing and balance are both transmitted by the vestibulocochlear nerve (VIII). This nerve functions as two separate nerves, carrying information from two separate but closely related structures. The cochlear nerve is the portion of the vestibulocochlear nerve involved in hearing; the vestibular nerve is involved in balance. Figure 9.23 illustrates the neuronal pathways for hearing.

PROCESS Figure

PROCESS Figure 9.23 **Neuronal Pathways for Hearing**

Action potentials generated at the spiral organ are conducted to the temporal lobes of the cerebrum.

Cochlear implants are devices that can be used to restore hearing in some individuals. The implant includes a small device that detects sound and then transmits the sound to the inner ear. Within the inner ear, the implant stimulates the cochlear nerve through electrical impulses. Why are cochlear implants not ideal for all types of deafness?

❶ The cochlear nerve sends axons to the **cochlear nucleus** in the brainstem.

❷ Neurons in the cochlear nucleus project to other areas of the brainstem and to the **inferior colliculus** in the midbrain. Neurons from the

inferior colliculus also project to the superior colliculus, where reflexes that turn the head and eyes in response to loud sounds are initiated.

❸ From the inferior colliculus, fibers project to the thalamus.

❹ Neurons of the thalamus project to auditory cortex in the temporal lobe of each cerebral hemisphere.

Balance

The sense of balance, or equilibrium, has two components: (1) static equilibrium and (2) dynamic equilibrium. **Static equilibrium** is associated with the vestibule and is involved in evaluating the position of the head relative to gravity. **Dynamic equilibrium** is associated with the semicircular canals and is involved in evaluating changes in the direction and rate of head movements.

The **vestibule** (VES-tih-byul) of the inner ear can be divided into two chambers: (1) the **utricle** (YOU-tri-kul) and (2) the **saccule** (SAK-yool) (figure 9.24*a*). Each chamber contains specialized patches of epithelium called the **maculae** (MAK-you-lee), which are surrounded by endolymph. The maculae, like the spiral organ, contain hair cells. The tips of the microvilli of these cells are embedded in a gelatinous mass, often called the *otolithic membrane*. The membrane is weighted by **otoliths** (OH-toh-liths; oto -, ear; lith-, stone), which are particles composed of protein and calcium carbonate. The weighted gelatinous mass moves in response to gravity, bending the hair cell microvilli (figure 9.24*c*) and initiating action potentials in the associated neurons. The action potentials from these neurons are carried by axons of the vestibular portion of the vestibulocochlear nerve (VIII) to the brain, where they are interpreted as a change in the position of the head. For example, when a person bends over, the maculae are displaced by gravity, and the resultant action potentials provide information to the brain concerning the position of the head (figure 9.25).

Figure 9.24 APR **Location and Structure of the Macula**

(*a*) Location of the utricular and saccular maculae within the vestibule. (*b*) Enlargement of the utricular macula, showing hair cells and otoliths. (*c*) Enlarged hair cell, showing the microvilli. (*d*) Colorized scanning electron micrograph of otoliths.

(d) Susumu Nishinag/Science Source

Figure 9.25 **Function of the Vestibule in Maintaining Balance**

(*a*) In an upright position, the maculae don't move. (*b*) When the position of the head changes, as when a person bends over, the maculae respond by moving in the direction of gravity.

(a, b) ©Trent Stephens

The **semicircular canals** are involved in dynamic equilibrium. There are three semicircular canals in each ear. The semicircular canals are placed at nearly right angles to one another, enabling a person to detect movements in essentially any direction. The base of each semicircular canal is expanded into an **ampulla** (am-PUL-ah) (figure 9.26*a*). Within each ampulla, the epithelium is specialized to form a **crista ampullaris** (KRIS-tah am-pyoo-LAIR-is) (figure 9.26*b*). Each crista consists of a ridge of epithelium with a curved, gelatinous mass, the **cupula** (KOO-poo-lah; a tub), suspended over the crest. The cupula is structurally and functionally very similar to the maculae, except that it contains no otoliths. The hairlike microvilli of the crista hair cells (figure 9.26*c*) are embedded in the cupula. The cupula functions as a float that is displaced by endolymph movement within the semicircular canals (figure 9.27). As the head begins to move in one direction, the endolymph tends to remain stationary, while the cupula moves with the head. This difference displaces the cupula in a direction opposite that of the movement of the head. As movement continues, the fluid "catches up." When movement of the head and the cupula stops, the fluid continues to move, displacing the cupula in the direction of the movement. Movement of the cupula causes the hair cell microvilli to bend, which initiates depolarization in the hair cells. This depolarization initiates action potentials in the vestibular nerves, which join the cochlear nerves to form the vestibulocochlear nerves.

Figure 9.26 **Semicircular Canals**

(a) Location of the ampullae of the semicircular canals. (b) Enlargement of the crista ampullaris, showing the cupula and hair cells. (c) Enlargement of a hair cell.

Figure 9.27 **Function of the Crista Ampullaris**

(*a*) As a person begins to tumble, the semicircular canals (*b*) move in the same direction as the body (large blue arrow at the bottom of the figure). The endolymph in the semicircular canals tends to stay in place as the body and the crista ampullaris begin to move. As a result, the cupula is displaced by the moving endolymph (large *red arrow* at the top of the figure) in a direction opposite the direction of movement.

(a) Julie Jacobson/AP Images

Continuous stimulation of the semicircular canals—as occurs due to the rocking motion of a boat—can cause **motion sickness,** characterized by nausea and weakness. The brain compares sensory input from the semicircular canals, eyes, and position receptors (proprioceptors) in the back and lower limbs. Conflicting input from these sources can lead to motion sickness.

Apply It 7

Explain why closing your eyes or looking at the horizon can help decrease motion sickness.

Neuronal Pathways for Balance

Axons forming the vestibular portion of the vestibulocochlear nerve project to the vestibular nucleus in the brainstem. Axons run from this nucleus to numerous areas of the CNS, such as the cerebellum and cerebral cortex. Balance is a complex sensation involving sensory input to the vestibular nucleus not only from the inner ear but also from the limbs (proprioception) and visual system as well. In sobriety tests, people are asked to close their

eyes while their balance is evaluated because alcohol affects the proprioceptive and vestibular components of balance to a greater extent than the visual component of balance. Seasickness is a form of motion sickness, which is caused by conflicting information reaching the brain from different sensory sources, such as the eyes and the semicircular canals of the inner ear. The brain reacts with a feeling of vertigo (a feeling of spinning) and nausea.

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EFFECTS OF AGING ON SENSES

As a person ages, both the general and the special sensory functions gradually decline. Among the general senses, free nerve endings and hair follicle receptors in the skin remain largely unchanged. However, the numbers of Meissner corpuscles and Pacinian corpuscles decrease with age, and those that remain are

often structurally distorted and less functional. As a result, elderly people are less conscious of something touching or pressing the skin, which increases the risk of skin injuries. The sense of two-point discrimination decreases, and the elderly have a more difficult time identifying objects by touch. A loss of Pacinian corpuscles also decreases their awareness of limb and joint positions, which can affect balance and coordination. The functions of receptors for proprioception also decline with age, which decreases information on the position, tension, and length of tendons and muscles. This can further reduce coordination and control of movements.

Among the special senses, elderly people experience only a slight loss in the ability to detect odors. However, their ability to correctly identify specific odors decreases, especially in men over age 70.

In general, the sense of taste decreases as people age. The number of sensory receptors decreases, and the brain's ability to interpret taste sensations declines.

The lenses of the eyes lose flexibility as a person ages because the connective tissue of the lenses becomes more rigid. Consequently, the lenses' ability to change shape initially declines and eventually is lost. This condition, called **presbyopia,** is the most common age-related change in the eyes. In addition, the number of cones decreases, especially in the fovea centralis, resulting in a gradual decline in visual acuity and color perception.

The most common visual problem in older people requiring medical treatment, such as surgery, is the development of cataracts. Following cataracts in frequency are macular degeneration, glaucoma, and diabetic retinopathy, in that order (see table 9.1).

As people age, the number of hair cells in the cochlea decreases, resulting in age-related sensorineural hearing loss, called **presbyacusis.** This decline doesn't occur equally in both ears. Therefore, because direction is determined by comparing sounds coming into each ear, elderly people may experience a decreased ability to localize the origin of certain sounds. This may lead to a general sense of disorientation. In addition, CNS defects in the auditory pathways can lead to difficulty understanding sounds when echoes or background noises are present. This deficit makes it difficult for elderly people to understand rapid or broken speech.

With age, the number of hair cells in the saccule, utricle, and ampullae decreases. The number of otoliths also declines. As a result, elderly people experience a decreased sensitivity to gravity, acceleration, and rotation, which may lead to disequilibrium (instability) and vertigo (a feeling of spinning). Some elderly people feel that they can't maintain posture and are prone to fall.

Table 9.1 REPRESENTATIVE DISEASES AND DISORDERS: Vision, Hearing, and Balance

Condition	Description
	EYE DISORDERS
Infections	
Trachoma (trah-KOH-mah)	Type of conjunctivitis caused by *Chlamydia*; leading cause of infectious blindness in the world; transmitted by contact or flies
Stye (st-eye)	Infection of eyelash hair follicle
Defects of Focus, Alignment, or Color Vision	
Myopia (my-OH-pee-ah)	Nearsightedness—ability to see close but not distant objects; caused when refractive power of cornea and lens is too great relative to length of eye
Hyperopia (high-per-OH-pee-ah)	Farsightedness—ability to see distant but not close objects; caused when cornea is too flat or lens has too little refractive power relative to length of eye
Astigmatism (ah-STIG-mah-tiz-em)	Cornea or lens is not uniformly curved, so image is not sharply focused
Strabismus (stra-BIZ-muss)	One or both eyes are misdirected; can result from weak eye muscles
Blindness	
Cataract (KAT-ah-rakt)	Clouding of lens as a result of advancing age, infection, or trauma; most common cause of blindness in the world
Macular degeneration	Loss of sharp central vision, peripheral vision maintained; leading cause of legal blindness in older Americans; most causes not known
Diabetic retinopathy	Involves optic nerve degeneration, cataracts, retinal detachment; often caused by blood vessel degeneration and hemorrhage

Condition	Description
Retinal detachment	Separation of sensory retina from pigmented retina; relatively common problem; may result in vision loss
	EAR DISORDERS
Tinnitus (ti-NYE-tus)	Phantom sound sensations, such as ringing in ears; common problem
Meniere disease	Vertigo, hearing loss, tinnitus, and a feeling of fullness in the affected ear; most common disease involving dizziness from inner ear; cause unknown but may involve a fluid abnormality in ears

SUMMARY

9.1 Sensation

Perception of sensations results only from those stimuli that reach the cerebral cortex and are consciously perceived. Senses can be defined as general or special.

9.2 Sensory Receptors

Sensory receptors are sensory nerve endings or specialized cells capable of responding to stimuli by developing action potentials.

9.3 General Senses

Receptors for general senses, such as pain, temperature, touch, pressure, and proprioception, are scattered throughout the body.

Pain

1. Pain is an unpleasant sensation that may be either localized or diffuse.
2. Pain can be reduced or controlled by stimulation of tactile receptors as well as increased motor activity.
3. Pain from deeper structures may be referred to more superficial structures, such as the skin.

9.4 Special Senses

Smell and taste respond to chemical stimulation, vision to light stimulation, and hearing and balance to mechanical stimulation.

9.5 Olfaction

1. Olfactory neurons have enlarged distal ends with long cilia. The cilia have receptors that respond to dissolved substances in the nasal mucus.
2. The wide range of detectable odors results from combinations of receptor responses.

Neuronal Pathways for Olfaction

Axons of the olfactory neurons form the olfactory nerves, which enter the olfactory bulb. Olfactory tracts carry action potentials from the olfactory bulbs to the olfactory cortex of the brain.

9.6 Taste

1. Taste buds contain taste cells with hairs that extend into taste pores. Receptors on the hairs detect dissolved substances.
2. There are five basic types of taste: sour, salty, bitter, sweet, and umami.

Neuronal Pathways for Taste

The facial nerve carries taste from the anterior two-thirds of the tongue; the glossopharyngeal nerve carries taste from the posterior one-third of the tongue; and the vagus nerve carries taste from the root of the tongue.

9.7 Vision

Accessory Structures of the Eye

1. The eyebrows prevent perspiration from entering the eyes.
2. The eyelids protect the eyes from foreign objects.
3. The conjunctiva covers the inner eyelids and the anterior surface of the eye.
4. Lacrimal glands produce tears that flow across the eye surface to lubricate and protect the eye. Excess tears pass through the nasolacrimal duct into the nasal cavity.
5. The extrinsic eye muscles move the eyeball.

Anatomy of the Eye

1. The fibrous tunic is the outer layer of the eye. It consists of the sclera and cornea.
2. The vascular tunic is the middle layer of the eye. It consists of the choroid, ciliary body, and iris.
3. The lens is held in place by the suspensory ligaments, which are attached to the smooth muscles of the ciliary body.
4. The nervous tunic (retina) is the inner layer of the eye and contains neurons sensitive to light.
5. Rods are responsible for vision in low illumination (night vision).
6. Cones are responsible for color vision.
7. The fovea centralis in the center of the macula has the highest concentration of cones and is the area where images are detected most clearly.
8. The optic disc, or blind spot, is where the optic nerve exits the eye and blood vessels enter.
9. The anterior and posterior chambers of the eye are anterior to the lens and are filled with aqueous humor. The vitreous chamber is filled with vitreous humor. The humors keep the eye inflated, refract light, and provide nutrients to the inner surface of the eye.

Functions of the Eye

1. Light passing through a concave surface diverges. Light passing through a convex surface converges.
2. Converging light rays cross at the focal point and are said to be focused.
3. The cornea, aqueous humor, lens, and vitreous humor all refract light. The cornea is responsible for most of the convergence, whereas the lens can adjust the focus by changing shape (accommodation).
4. Light causes retinal to change shape, which causes opsin to change shape, leading eventually to cellular changes that result in an action potential at the retina.
5. Action potentials are conducted along the optic nerve.

Neuronal Pathways for Vision

1. Axons pass through the optic nerves to the optic chiasm, where some cross. Axons from the nasal retina cross, and those from the temporal retina do not.

2. Optic tracts from the chiasm lead to the thalamus.
3. Optic radiations extend from the thalamus to the visual cortex in the occipital lobe.

9.8 Hearing and Balance

Anatomy and Function of the Ear

1. The external ear consists of the auricle and the external auditory canal.
2. The middle ear contains the three auditory ossicles.
3. The tympanic membrane (eardrum) is stretched across the external auditory canal.
4. The malleus, incus, and stapes connect the tympanic membrane to the oval window of the inner ear.
5. The auditory, or eustachian, tube connects the middle ear to the pharynx and equalizes pressure. The middle ear is also connected to the mastoid air cells.

6. The inner ear has three parts: the semicircular canals, the vestibule, and the cochlea.
7. The cochlea is a canal shaped like a snail's shell.
8. The cochlea is divided into three compartments by the vestibular and basilar membranes.
9. The spiral organ consists of hair cells that attach to the basilar and tectorial membranes.

Hearing

1. Sound waves are funneled through the auricle down the external auditory canal, causing the tympanic membrane to vibrate.
2. The tympanic membrane vibrations are passed along the ossicles to the oval window of the inner ear.
3. Movement of the stapes in the oval window causes the perilymph to move the vestibular membrane, which causes the endolymph to move the basilar membrane. Movement of the basilar membrane causes the hair cells in the spiral organ to move and generate action potentials, which travel along the vestibulocochlear nerve.

Neuronal Pathways for Hearing

From the vestibulocochlear nerve, action potentials travel to the cochlear nucleus and on to the cerebral cortex.

Balance

1. Static equilibrium evaluates the position of the head relative to gravity.
2. Maculae, located in the vestibule, consist of hair cells with the microvilli embedded in a gelatinous mass that contains otoliths.
   The gelatinous mass moves in response to gravity.
3. Dynamic equilibrium evaluates movements of the head.
4. The inner ear contains three semicircular canals, arranged perpendicular to each other. The ampulla of each semicircular canal contains a crista ampullaris, which has hair cells with microvilli embedded in a gelatinous mass, the cupula.

Neuronal Pathways for Balance

Axons in the vestibular portion of the vestibulocochlear nerve project to the vestibular nucleus and on to the cerebral cortex.

REMEMBERING AND UNDERSTANDING

1. Describe how a stimulus becomes a sensation.
2. Contrast the features of the receptors associated with the general senses.
3. Explain how pain is reduced by analgesics and how it can be modified, according to the gate control theory.
4. Explain referred pain, and give an example.
5. Describe the process by which airborne molecules produce the sensation of smell.
6. How is the sense of taste related to the sense of smell?

7. What are the five primary tastes? How do they produce many different kinds of taste sensations?
8. Describe the following structures and state their functions: eyebrows, eyelids, conjunctiva, lacrimal apparatus, and extrinsic eye muscles.
9. Name the three tunics of the eye. Describe the structures composing each layer, and explain the functions of these structures.
10. Describe the three chambers of the eye, the substances that fill each, and the functions of these substances.
11. Describe the lens of the eye and how it is held in place.
12. Describe the arrangement of rods and cones in the fovea centralis and in the periphery of the eye.
13. What causes the pupil to constrict and dilate?
14. What is the blind spot of the eye, and what causes it?
15. What causes light to refract? What is a focal point?
16. Define accommodation. What does accommodation accomplish?
17. Name the three regions of the ear, name the structures in each region, and state the functions of each structure.
18. Describe the relationship among the tympanic membrane, the auditory ossicles, and the oval window of the inner ear.
19. Describe the structure of the cochlea.
20. Starting with the auricle, trace sound into the inner ear to the point at which action potentials are generated in the vestibulocochlear nerve.
21. Describe the maculae in the vestibule of the ear and their function in balance.
22. What is the function of the semicircular canals? Describe the crista ampullaris and its mode of operation.

CRITICAL THINKING

1. An elderly male with normal vision developed cataracts. A surgeon treated his condition by removing the lenses of his eyes. What aspect of his vision will be most affected by the removal of the lenses? Explain your answer.

2. On a camping trip, Stephanie was admiring the stars in the night sky. She noticed a little cluster of dim stars at the edge of her vision, but when she looked directly at that part of the sky, she could not see the cluster. On the other hand, when she looked toward the stars but not directly at them, she could see them. Explain what was happening.
3. SCUBA divers are subject to increased pressure as they descend toward the bottom of the ocean. Sometimes this pressure can lead to damage to the ear and loss of hearing. Describe the normal mechanisms that adjust for changes in pressure. Explain how increased pressure might cause reduced hearing, and suggest at least one other common condition that might interfere with this pressure adjustment.
4. If a vibrating tuning fork were placed against the mastoid process of your temporal bone, you would perceive the vibrations as sound, even if the external auditory canal were plugged. Explain how this happens.
5. The main way that people "catch" colds is through their hands. After touching an object contaminated with the cold virus, the person transfers the virus to the nasal cavity, where it causes an infection. Other than the obvious entry of the virus through the nose, how could the virus get into the nasal cavity?

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

10

Endocrine System

The endocrine system is essential for the body to maintain homeostasis.

LEARN TO APPLY IT

Katie was getting nervous. At 16, she was the only one in her group of friends who had not started menstruating. Katie had always dreamed of having three beautiful children someday and she was worried. Her mother took her to see Dr. Josephine, who ordered several blood tests. When the results came back, Dr. Josephine gently explained to Katie and her mother that Katie would never be able to have children and would never menstruate. Dr. Josephine then asked Katie to wait in the outer room while she spoke privately to her mother. She explained to Katie's mom that Katie had Androgen Insensitivity Syndrome. Though Katie was genetically male and her gonads produced more of the male reproductive hormone, testosterone, than the female reproductive hormone, estrogen, Katie did not reflect the tissue changes expected.

What malfunction in Katie's body would cause this? Why does Katie's body look feminine if she is genetically male?

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 8 Endocrine System

10.1 PRINCIPLES OF CHEMICAL COMMUNICATION

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the four classes of chemical messengers.
B. Define hormone and target tissue.
C. Distinguish between endocrine and exocrine glands.

Characteristics of the Endocrine System

The **endocrine system** is composed of **endocrine glands** and specialized endocrine cells located throughout the body (figure 10.1). Endocrine glands and cells secrete very small amounts of chemical messengers called **hormones** (HOR-mohns; to excite) into the extracellular fluid. The hormones diffuse into the blood to be transported to their target. Hormones circulate through the bloodstream to specific sites called **target tissues** or *effectors*. At their target tissues, hormones stimulate a specific response. Thus, the term **endocrine** (EN-doh-krin) —derived from the Greek words endo, meaning "within," and *krino*, "to secrete"—appropriately describes this system.

Figure 10.1 APR **Major Endocrine Glands and Their Locations**

The major endocrine glands are: pineal gland, pituitary, thyroid, parathyroids, thymus, adrenals, pancreas, ovaries, and testes.

Endocrine glands are not to be confused with **exocrine glands.** Exocrine glands have ducts that carry their secretions to the outside of the body, or into a hollow organ, such as the stomach or intestines. Examples of exocrine secretions are saliva, sweat, breast milk, and digestive enzymes.

The study of the endocrine system, known as **endocrinolog,** is the topic of this chapter. In this chapter, we present the general principles of hormones and we discuss specific hormones and their functions. Hormones have a role in most physiological processes in the body.

Classes of Chemical Messengers

The body has a remarkable capacity for maintaining homeostasis despite having to coordinate the activities of nearly 40 trillion cells. The principal means by which this coordination occurs is through chemical messengers, some produced by the nervous system and others produced by the endocrine system. **Chemical messengers** allow cells to communicate with each other to regulate body activities.

Most chemical messengers are produced by a specific collection of cells or by a gland. Recall from chapter 4 that a gland is an organ consisting of epithelial cells that specialize in **secretion,** which is the controlled release of chemicals from a cell. This text identifies four classes of chemical messengers based on the source

of the chemical messenger and its mode of transport in the body (table 10.1). In this section, we describe chemical messengers in terms of how they function. But it is important to note that some chemical messengers fall into more than one functional category. For example, prostaglandins are listed in multiple categories because they have diverse functions and cannot be categorized in just one class. Therefore, the study of the endocrine system includes several of the following categories:

1. *Autocrine chemical messengers.* An autocrine (*auto-*, self) chemical messenger stimulates the cell that originally secreted it. Good examples of autocrine chemical messengers are those secreted by white blood cells during an infection. Several types of white blood cells can stimulate their own replication so that the total number of white blood cells increases rapidly (see chapter 14).
2. *Paracrine chemical messengers.* Paracrine (*para-*, next to) chemical messengers act locally on neighboring cells. These chemical messengers are secreted by one cell type into the extracellular fluid and affect surrounding cells. An example of a paracrine chemical messenger is histamine, released by certain white blood cells during allergic reactions. Histamine stimulates vasodilation in nearby blood vessels.
3. *Neurotransmitters.* Neurotransmitters are chemical messengers secreted by neurons that activate an adjacent cell, whether it is another neuron, a muscle cell, or a glandular cell. Neurotransmitters are secreted into a synaptic cleft, rather than into the bloodstream (see chapter 8). Therefore, in the strictest sense neurotransmitters are paracrine chemical messengers, but for our purposes it is most appropriate to consider them as a separate category.
4. *Endocrine chemical messengers.* Endocrine (*endo-*, within) chemical messengers are secreted into the bloodstream by certain glands and cells, which together constitute the endocrine system. These chemical messengers travel through the blood to their target cells.

TABLE 10.1 Classes of Chemical Messengers

Chemical Messenger	Description	Example
Autocrine	Secreted by cells in a local area; influences the activity of the same cell or cell type from which it was secreted	Eicosanoids (prostaglandins, thromboxanes, prostacyclins, leukotrienes)

Chemical Messenger	Description	Example	
Paracrine	Produced by a wide variety of tissues and secreted into extracellular fluid; has a localized effect on other tissues	Somatostatin, histamine, eicosanoids	
Neurotransmitter	Produced by neurons; secreted into a synaptic cleft by presynaptic nerve terminals; travels short distances; influences postsynaptic cells	Acetylcholine, epinephrine	
Endocrine	Secreted into the blood by specialized cells; travels some distance to target tissues; results in coordinated regulation of cell function	Thyroid hormones, growth hormone, insulin, epinephrine, estrogen, progesterone, testosterone, prostaglandins	

10.2 FUNCTIONS OF THE ENDOCRINE SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Explain the types of information that are necessary to understand endocrine function.
B. Describe the ten regulatory functions of the endocrine system.

The endocrine system is one of the two important control systems of the body. The nervous system is the body's other important control system (see figure 10.1).

Hormones of the endocrine system are secreted in response to humoral, neural, or hormonal stimuli to regulate homeostasis. In order to understand completely how the endocrine system regulates body functions, you need to know the various endocrine glands, their hormones, and their mechanisms of action. In addition, many disorders of the body are caused by either hypersecretion or hyposecretion of hormones.

The main regulatory functions of the endocrine system are the following:

1. *Regulation of metabolism.* Controls the rate of nutrient utilization and energy production.

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2. *Control of food intake and digestion.* Regulates the level of satiation (fullness) and the breakdown of food into individual nutrients.
3. *Modulation of tissue development.* Influences the development of tissues, such as those of the nervous system.
4. *Regulation of ion levels.* Helps monitor blood pH, as well as Na^+, K^+, and Ca^{2+} concentrations in the blood.
5. *Control of water balance.* Regulates water balance by controlling the solute concentration of the blood as well as controlling membrane permeability.
6. *Regulation of cardiovascular functions.* Helps regulate the heart rate and blood pressure and prepare the body for physical activity.
7. *Control of blood glucose and other nutrients.* Regulates the levels of glucose and other nutrients in the blood.
8. *Control of reproductive functions.* Controls the development and functions of the reproductive systems in males and females.
9. *Stimulation of uterine contractions and milk release.* Regulates uterine contractions during delivery and stimulates milk release from the breasts in lactating females.
10. *Modulation of immune system function.* Helps control the production of immune cells.

10.3 HORMONES

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the common characteristics of all hormones.
B. List and describe the two chemical categories of hormones.
C. Explain the influence of the chemical nature of a hormone on its transport in the blood, its removal from the blood, and its life span.
D. Describe the three main patterns of hormone secretion.

The word *hormone* is derived from the Greek word *hormon,* which means to "set into motion." Hormones are very powerful molecules.

Chemical Nature of Hormones

Hormones fit into one of two chemical categories: (1) lipid-soluble hormones and (2) water-soluble hormones, a distinction based on their chemical composition, which influences their chemical behavior. Recall from chapter 3 that the cell membrane is a selectively permeable phospholipid bilayer that excludes most water-soluble molecules but allows lipid-soluble molecules to pass through. Therefore, the entire basis of a hormone's metabolism—its transport in the blood, its interaction with its target, and its removal from the body—is dependent on the hormone's chemical nature.

Within the two chemical categories, hormones can be subdivided into groups based on their chemical structures. Steroid hormones are those derived from cholesterol, thyroid hormones are derived from the amino acid tyrosine, and other hormones are categorized as amino acid derivatives, peptides, or proteins.

Lipid-Soluble Hormones

Lipid-soluble hormones are nonpolar, and include steroid hormones, thyroid hormones, and fatty acid derivative hormones, such as certain eicosanoids.

Transport of Lipid-Soluble Hormones

Because of their small size and low solubility in aqueous fluids, if lipid-soluble hormone molecules circulated in the blood unprotected, they could be easily removed from the blood and would be unable to effectively regulate their targets. There are at least three mechanisms that could potentially result in the removal of unprotected lipid-soluble hormones from the body: (1) breakdown by enzymes in the liver or enzymes in the lungs, (2) excretion into urine by the kidneys, and (3) breakdown by enzymes in the bloodstream. Hormones that are degraded by enzymes in the blood would then be excreted in the urine or in bile produced in the liver.

Fortunately, lipid-soluble hormones are not unprotected. Instead, they travel in the bloodstream bound to **binding proteins** (figure 10.2). Binding proteins "chaperone" the hormone. This binding significantly reduces the rate at which lipid-soluble hormones are degraded or removed from the blood. The life span of lipid-soluble hormones in the blood typically ranges from a few days to several weeks. Eventually, even though lipid-soluble hormones are bound to binding proteins, they are still removed from the plasma through excretion in urine from the kidney or bile from the liver (bile enters the digestive tract).

Figure 10.2 **Effects of Binding Proteins**

Free hormones (those that circulate freely in the blood) immediately activate target cells once they are delivered from the blood. The blood levels of these hormones tend to fluctuate to a greater degree than the levels of hormones that attach to binding proteins. Water-soluble hormones then bind to their receptors, which are membrane-bound in the target cell. Hormones that are transported in the blood attached to binding proteins circulate in the blood as bound or free hormones. As the concentration of free hormones decreases, bound hormones are released from the binding proteins. This provides a chronic, stable supply of hormones and, thus, more-consistent control of target cells. This is especially important for hormones that regulate basal metabolism. Lipid-soluble hormones bind their receptors in either the cytoplasm or the nucleus.

Water-Soluble Hormones

Water-soluble hormones are polar molecules; they include protein hormones, peptide hormones, and most amino acid derivative hormones.

Transport of Water-Soluble Hormones

Because water-soluble hormones can dissolve in blood, many circulate as free hormones, meaning that most of them dissolve directly into the blood and are delivered to their target tissue without attaching to a binding protein (see figure 10.2). Because many water-soluble hormones are quite large, they do not readily diffuse through the walls of all capillaries; therefore, they tend to diffuse from the blood into tissue spaces more slowly. Organs regulated by some protein hormones have very porous, or *fenestrated*, capillaries to aid in delivery of these hormones to individual cells (see chapter 13). On the other hand, other water-soluble hormones are quite small and are attached to a binding protein to avoid being filtered out of the blood.

All hormones are destroyed either in the blood or at their target cells. The destruction and elimination of hormones limit the length of time they are active,

and body processes change quickly when hormones are secreted and remain functional for only short periods.

The water-soluble hormones have relatively short half-lives because they are rapidly broken down by enzymes within the bloodstream. The kidneys then remove the hormone breakdown products from the blood. Target cells can also destroy water-soluble hormones. Once the hormones are inside the target cell, lysosomal enzymes degrade them. Often the target cell recycles the amino acids of peptide and protein hormones and uses them to synthesize new proteins. Thus, hormones with short half-lives normally have concentrations that change rapidly within the blood and tend to regulate activities that have a rapid onset and short duration.

However, some water-soluble hormones are more stable in the blood than others. There are many modifications made to hormone molecules that help protect them from being destroyed. Three important modifications include:

1. Having a carbohydrate attached to them.
2. Having a terminal end protected from protease activity.
3. Having binding proteins. Bound hormones circulate in the plasma longer than free water-soluble hormones do.

10.4 CONTROL OF HORMONE SECRETION

Learning Outcomes *After reading this section, you should be able to*

A. List and describe the three stimulatory influences on hormone secretion and give examples.
B. List and describe the three inhibitory influences on hormone secretion and give examples.
C. Describe the major mechanisms that maintain blood hormone levels.

Three types of stimuli regulate hormone release: (1) humoral, (2) neural, and (3) hormonal. No matter what stimulus causes the release of the hormone, however, the blood level of most hormones fluctuates within a homeostatic range through negative-feedback mechanisms (see chapter 1). In a few instances, positive-feedback systems also regulate blood hormone levels.

Stimulation of Hormone Release

Control by Humoral Stimuli

Molecules and ions in the bloodstream can directly stimulate the release of some hormones. These chemicals are referred to as **humoral stimuli.** The word *humoral* refers to body fluids, including blood. The cells that secrete these hormones have receptors for certain substances in the blood. For example, calcium stimulates the release of the hormone PTH. Figure 10.3 illustrates that when the blood level of a particular chemical changes (calcium), the hormone (PTH) is released in response to the chemical's concentration. Other examples

include elevated blood glucose levels directly stimulating the pancreas to secrete the hormone insulin, and elevated blood potassium levels directly stimulating the adrenal cortex to secrete the hormone aldosterone.

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Figure 10.3 APR **Humoral Regulation of Hormone Secretion**
Some hormones are released when the blood levels of a certain chemical changes. For example, if blood Ca^{2+} levels decrease, PTH is secreted. If blood Ca^{2+} levels increase, PTH secretion slows. Some hormones are secreted in direct response to changes in certain blood-borne chemicals, such as Ca^{2+}.

Control by Neural Stimuli

The second type of hormone regulation involves **neural stimuli** of endocrine glands. Figure 10.4 illustrates the neural control of hormone secretion from cells of an endocrine gland.

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PROCESS Figure

PROCESS Figure 10.4 Control of Hormone Secretion by Direct Neural Innervation

Some hormone secretion is due to a stimulus from a neurotransmitter.

What cell membrane component must the endocrine cell have, in order to respond to a neurotransmitter?

❶ Following action potentials, neurons release a neurotransmitter into the synapse with the cells that produce the hormone.

❷ In some cases, the neurotransmitter stimulates the cells to increase hormone secretion.

For example, the sympathetic nervous system (see chapter 8) stimulates the secretion of epinephrine and norepinephrine, from the adrenal gland during exercise. Epinephrine and norepinephrine increase heart rate and, in turn, increase blood flow through the exercising muscles. When the exercise stops, the neural stimulation declines and the secretion of epinephrine and norepinephrine decreases.

Some neurons secrete chemical messengers directly into the blood when they are stimulated, making these chemical messengers hormones, which are called

neuropeptides. Specialized neuropeptides stimulate hormone secretion from other endocrine cells and are called **releasing hormones,** a term usually reserved for hormones from the hypothalamus.

Control by Hormonal Stimuli

The third type of regulation uses **hormonal stimuli.** It occurs when a hormone is secreted that, in turn, stimulates the secretion of other hormones. The most common examples are hormones from the anterior pituitary gland, called **tropic** (TROH-pik) **hormones.** Tropic hormones are hormones that stimulate the secretion of another hormone. Figure 10.5 illustrates hormone secretion from the hypothalamus and pituitary, which is regulated by hormonal stimuli.

PROCESS Figure

PROCESS Figure 10.5 **Hormonal Regulation of Hormone Secretion**
Some hormone secretion is due to a stimulus from another hormone.

What type of hormonal secretion mechanism is found in step 1?

❶ Neurons in the hypothalamus release stimulatory hormones, called releasing hormones. Releasing hormones travel in the blood to the anterior pituitary

gland.

❷ Releasing hormones stimulate the release of hormones from the anterior pituitary that travel in the blood to their target endocrine cell.

❸ The target endocrine cell secretes its hormone into the blood, where it travels to its target and produces a response.

Inhibition of Hormone Release

Stimulating hormone secretion is important, but inhibiting hormone release is also important. This process involves the same three types of stimuli: (1) humoral, (2) neural, and (3) hormonal.

Inhibition of Hormone Release by Humoral Stimuli

Often when a hormone's release is sensitive to the presence of a humoral stimulus, there exists a companion hormone whose release is inhibited by the same humoral stimulus. Usually, the companion hormone's effects oppose those of the secreted hormone and counteract the secreted hormone's action. For example, to raise blood pressure, the adrenal cortex secretes the hormone aldosterone in response to low blood pressure. However, if blood pressure goes up, the atria of the heart secrete the hormone atrial natriuretic peptide (ANP), which lowers blood pressure. Therefore, aldosterone and ANP work together to maintain homeostasis of blood pressure.

Inhibition of Hormone Release by Neural Stimuli

Neurons inhibit targets just as often as they stimulate targets. If the neurotransmitter is inhibitory, the target endocrine gland does not secrete its hormone.

Inhibition of Hormone Release by Hormonal Stimuli

Some hormones prevent the secretion of other hormones, which is a common mode of hormone regulation. For example, hormones from the hypothalamus that prevent the secretion of tropic hormones from the anterior pituitary gland are called **inhibiting hormones.** Thyroid hormones can control their own blood levels by inhibiting their anterior pituitary tropic hormone. Without the original stimulus, less thyroid hormone is released.

Regulation of Hormone Levels in the Blood

Two major mechanisms maintain hormone levels in the blood within a homeostatic range: (1) negative feedback and (2) positive feedback (see chapter 1).

Negative Feedback

Most hormones are regulated by a negative-feedback mechanism, whereby the hormone's secretion is inhibited by the hormone itself once blood levels have reached a certain point and there is adequate hormone to activate the target cell. The hormone may inhibit the action of other, stimulatory hormones to prevent the secretion of the hormone in question. Thus, it is a self-limiting system.

For example, thyroid hormones inhibit the secretion of their releasing hormone from the hypothalamus and their tropic hormone from the anterior pituitary.

The steps for the thyroid hormone negative-feedback system are shown in figure 10.6*a*.

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PROCESS Figure

PROCESS Figure 10.6 **Negative and Positive Feedback**

Blood hormone levels are tightly regulated through negative and positive feedback.

Understand **What provides a negative feedback signal for a hormone that is regulated by a humoral stimulus? Explain.**

❶ The anterior pituitary gland secretes a tropic hormone, which travels in the blood to the target endocrine cell.

❷ The hormone from the target endocrine cell travels to its target.

❸ The hormone from the target endocrine cell also has a negative-feedback effect on the anterior pituitary and hypothalamus, which decreases secretion of the tropic hormone.

Positive Feedback

Some hormones, when stimulated by a tropic hormone, promote the synthesis and secretion of the tropic hormone in addition to stimulating their target cell. In turn, this stimulates further secretion of the original hormone. Thus, it is a self-propagating system.

For example, prolonged estrogen stimulation promotes a release of the anterior pituitary hormone responsible for stimulating ovulation.

The steps in the estrogen positive-feedback mechanism are shown in figure 10.6*b*.

❶ The anterior pituitary gland secretes a tropic hormone, which travels in the blood to the target endocrine cell.

❷ The hormone from the target endocrine cell travels to its target.

❸ The hormone from the target endocrine cell also has a positive-feedback effect on the anterior pituitary, which increases the secretion of the tropic hormone.

10.5 HORMONE RECEPTORS AND MECHANISMS OF ACTION

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the general properties of a receptor.

B. Explain the mechanisms of action for the two types of receptor classes.

C. Define amplification, and explain how, despite small hormone concentrations, water-soluble hormones can cause rapid responses.

Hormones exert their actions by binding to target cell proteins called **receptors.** A hormone can stimulate only the cells that have the receptor for that hormone. The portion of each receptor molecule where a hormone binds is called a **receptor site,** and the shape and chemical characteristics of each receptor site allow only a specific type of hormone to bind to it. The tendency for each type of hormone to bind to one type of receptor, and not to others, is called **specificity** (figure 10.7). For example, insulin binds to insulin receptors, but not to receptors for thyroid hormones. However, some hormones, such as epinephrine, can bind to a "family" of receptors that are structurally similar. Because hormone receptors have a high affinity for the hormones that bind to them, only a small concentration of a given hormone is needed to activate a significant number of its receptors.

Figure 10.7 **Target Tissue Specificity and Response**

Hormones bind to receptor proteins. The shape and chemical nature of each receptor site allow only a specific hormone to bind. This relationship is called specificity. Additionally, in order for a target cell to respond to its hormone, the hormone must bind to its receptor.

Classes of Receptors

Lipid-soluble and water-soluble hormones bind to their own classes of receptors. Figure 10.8 provides an overview of receptor type and mechanism of action.

Figure 10.8 **General Comparison of Nuclear and Membrane-Bound Receptors**

(*a*) *Lipid-soluble* hormones diffuse through the cell membrane of its target cell and bind to a cytoplasmic receptor or a nuclear receptor. In the nucleus, the combination of the hormone and the receptor initiates protein synthesis, described later in this chapter. (*b*) *Water-soluble* hormones bind to the external portion of membrane-bound receptors, which are integral membrane proteins on its target cell.

1. *Lipid-soluble hormones bind to nuclear receptors.* Lipid-soluble hormones are relatively small and are all nonpolar. Recall from chapter 3 that nonpolar molecules can freely cross the cell membrane. However, certain lipid-soluble hormones, in particular thyroid hormones, utilize membrane transporters to enter the target cell.

Once lipid-soluble hormones enter their target cell, they bind to **nuclear receptors,** which are most often found in the cell nucleus (figure 10.8*a*). Nuclear receptors can also be located in the cytoplasm, but then move to the nucleus when activated. When hormones bind to nuclear receptors, the hormone-receptor complex interacts with DNA in the nucleus or with cellular enzymes to regulate the transcription of particular genes in the target tissue, a process that takes several minutes to several hours. Thyroid hormones and steroid hormones (testosterone, estrogen, progesterone, aldosterone, and cortisol) generally bind to nuclear receptors.

In addition to modulating gene transcription, it is now recognized that lipid-soluble hormones have rapid effects (less than 1 minute) on target cells. These effects are most likely mediated through membrane-bound receptors (see next paragraph).

2. *Water-soluble hormones bind to membrane-bound receptors.* Water-soluble hormones are polar molecules and cannot pass through the cell membrane. Instead, they interact with **membrane-bound receptors,** which are proteins that extend across the cell membrane, with their hormone-binding sites exposed on the cell membrane's outer surface (figure 10.8*b*). When a hormone binds to a receptor on the outside of the cell membrane, the hormone-receptor complex initiates a response inside the cell. Hormones that bind to membrane-bound receptors include proteins, peptides, some amino acid derivatives, such as epinephrine and norepinephrine, and some lipid-soluble hormones.

Action of Nuclear Receptors

Primarily, lipid-soluble hormones stimulate protein synthesis. Figure 10.9 details the mechanism of action at nuclear receptors.

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PROCESS Figure

PROCESS Figure 10.9 APR **Nuclear Receptor Model**

Lipid-soluble hormones stimulate protein synthesis in their target cells.

Apply **Based on the characteristics of lipid-soluble hormones, explain why anabolic steroids can have numerous side effects.**

1. After lipid-soluble hormones enter their target cell they bind to their receptors.
2. Lipid-soluble hormones either bind to cytoplasmic receptors and travel to the nucleus or bind to nuclear receptors.
3. The hormone-receptor complex binds to DNA to produce new proteins. The receptors that bind to DNA have fingerlike projections that recognize and bind to specific nucleotide sequences in the DNA called **hormone-response elements.** The combination of the hormone and its receptor forms a **transcription factor.**

❹ When the hormone-receptor complex binds to the hormone-response element, it regulates the transcription of specific **messenger RNA (mRNA)** molecules.

❺ Newly formed mRNA molecules move to the cytoplasm of the cell, and bind to ribosomes to be translated into specific proteins.

❻ The new proteins produce the cell's response to the lipid-soluble hormone.

For example, testosterone stimulates the synthesis of proteins that are responsible for male sexual characteristics, such as the formation of muscle mass and the typical male body structure. The steroid hormone aldosterone affects its target cells in the kidneys by stimulating the synthesis of proteins that increase the rate of Na^+ and K^+ transport. The result is a reduction in the amount of Na^+ and an increase in the amount of K^+ lost in the urine. Other hormones that produce responses through nuclear receptor mechanisms include thyroid hormones and vitamin D.

Target cells that synthesize new protein molecules in response to hormonal stimuli normally have a latent period of several hours between the time the hormones bind to their receptors and the time responses are observed. During this latent period, mRNA and new proteins are synthesized. Hormone-receptor complexes are eventually degraded within the cell, limiting the length of time hormones influence the cells' activities, and the cells slowly return to their previous functional states.

Membrane-Bound Receptors and Signal Amplification

Recall from chapter 3 that the cell membrane contains proteins, which are embedded in the phospholipid bilayer. Membrane-bound receptors are types of membrane proteins. These receptors activate responses in two ways: (1) Some receptors alter the activity of G proteins at the inner surface of the cell membrane; (2) other receptors directly alter the activity of intracellular enzymes. These intracellular pathways elicit specific responses in cells, including the production of molecules called **second messengers.** A second messenger molecule is produced inside a cell once a hormone or another chemical messenger binds to certain membrane-bound receptors.

In response to the hormone, the second messenger then activates specific cellular processes inside the cell. In some cases, this coordinated set of events is referred to as a **second-messenger system.** For example, cyclic adenosine monophosphate (cAMP) (the second messenger) is a common second messenger produced when a ligand binds to its receptor. Rather than the ligand (the first messenger) entering the cell to directly activate a cellular process, the ligand stimulates cAMP (the second messenger) production. It is cAMP that then stimulates the cellular process. This mechanism is usually employed by water-soluble hormones that are unable to cross the target cell's membrane. It has also

been demonstrated that some lipid-soluble hormones activate second messenger systems, which is consistent with actions via membrane-bound receptors.

Membrane-Bound Receptors That Activate Adenylate Cyclase-Coupled G Proteins

Many membrane-bound receptors produce responses through the action of G proteins. G proteins consist of three subunits; from largest to smallest, they are called (1) alpha (α), (2) beta (β), and (3) gamma (γ). The G proteins are so named because one of the subunits binds to guanine nucleotides. In the inactive state, a guanine diphosphate (GDP) molecule is bound to the α subunit of each G protein. In the active state, guanine triphosphate (GTP) is bound to the α subunit. Figure 10.10 outlines the mechanism of action of membrane-bound receptors.

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PROCESS Figure

PROCESS Figure 10.10 APR **Membrane-Bound Receptors Activating G Proteins to Increase the Synthesis of cAMP**

Some G proteins initiate a cellular response through production of a second messenger, cAMP.

Certain stimulants, such as caffeine, work by increasing the levels of cAMP inside target cells. Based on the process shown here, what is a possible mechanism for caffeine stimulation?

1. Before the hormone binds to its receptor, the G protein freely floats in the cell membrane.
2. After a hormone binds to the receptor on the outside of a cell, the receptor changes shape and as a result, the receptor binds to a G protein. Guanine triphosphate (GTP) binds to the α subunit, thereby activating it.
3. The G proteins separate from the receptor, and the activated α subunit separates from the β and γ subunits. The activated α subunits activate **adenylate cyclase** (a-DEN-i-late CY-klase), an enzyme that converts ATP to cAMP.
4. Cyclic AMP functions as a second messenger. For example, cAMP binds to protein kinases and activates them. **Protein kinases** are enzymes that, in turn, regulate the activity of other enzymes. Protein kinases can either stimulate or inhibit the activity of the other enzyme.
5. The amount of time cAMP is present to produce a response in a cell is limited. An enzyme in the cytoplasm, called **phosphodiesterase** (FOS-foh-dy-ES-ter-ase), breaks down cAMP to AMP. Once cAMP levels drop, the enzymes in the cell are no longer stimulated.

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Cyclic AMP can elicit many different responses in the body because each cell type possesses a unique set of enzymes. For example, the hormone glucagon binds to receptors on the surface of liver cells, activating G proteins and causing an increase in cAMP synthesis, which stimulates the activity of enzymes that break down glycogen into glucose for release from liver cells (figure 10.10).

Signal Amplification

The rate and magnitude at which a hormone's response is stimulated are determined by its mechanism of action at the receptor. Nuclear receptors work by activating protein synthesis, which for some hormones can take several hours. However, hormones that stimulate the synthesis of second messengers can produce an almost instantaneous response because the second messenger influences existing enzymes. In other words, the response proteins are already present. Additionally, each receptor produces thousands of second messengers, leading to a cascade effect and ultimately **amplification** of the hormonal signal. With amplification, a single hormone activates many second messengers, each of which activates enzymes that produce an enormous amount of final product

(figure 10.11). The efficiency of this second-messenger amplification is virtually unparalleled in the body and can be thought of as an "army of molecules" launching an offensive. In a war, the general gives the signal to attack, and thousands of soldiers carry out the order. The general alone could not eliminate thousands of enemies. Likewise, one hormone could not single-handedly produce millions of final products within a few seconds. However, with amplification, one hormone has an army of molecules working simultaneously to produce the final products.

Figure 10.11 **Cascade Effect**

The combination of a hormone with a membrane-bound receptor activates several G proteins. The G proteins, in turn, activate many inactive adenylate cyclase enzymes, which cause the synthesis of a large number of cAMP molecules. The large number of cAMP molecules, in turn, activate many inactive protein kinase enzymes, which produce a rapid and amplified response.

Both nuclear receptor and membrane-bound receptor hormone systems are effective, but each is more suited to one type of response than another. For example, the reason epinephrine is effective in a fight-or-flight situation is that it can turn on the target cell responses within a few seconds. If running away from an immediate threat depended on producing new proteins, a process that can take several hours, many of us would have already perished. On the other hand, pregnancy maintenance is mediated by steroids, long-acting hormones, which is reflected by the fact that pregnancy is a long-term process. Thus, it is important that our bodies have hormones that can function over differing time scales.

Apply It 1

A drug binds to a receptor and prevents target tissues from responding to a hormone. It is known that the drug is lipid-soluble and that it prevents the synthesis of messenger RNA. Explain how the hormone produces a response in its target tissue.

10.6 ENDOCRINE GLANDS AND THEIR HORMONES

Learning Outcomes *After reading this section, you should be able to*

A. State the location of each of the endocrine glands in the body.
B. Describe how the hypothalamus regulates hormone secretion from the pituitary.
C. Describe how the pituitary gland regulates the secretion of hormones from other endocrine glands.
D. Choose a hormone and use it to explain how negative feedback results in homeostasis.
E. For each of the major hormones in the chapter, describe the endocrine gland from which it is secreted, its target tissue, the response of the target tissue, and the means by which its secretion is regulated.
F. List the effects of hyper- and hyposecretion of the major hormones.

The endocrine system consists of ductless glands that secrete hormones into the interstitial fluid (see figure 10.1). The hormones then enter the blood. Not surprisingly, the organs in the body with the richest blood supply are endocrine glands, such as the adrenal gland and the thyroid gland.

Some glands of the endocrine system perform functions in addition to hormone secretion. For example, the endocrine part of the pancreas has cells that secrete hormones, whereas the much larger exocrine portion of the pancreas secretes digestive enzymes. Portions of the ovaries and testes secrete hormones, but other parts of the ovaries and testes produce oocytes (female reproductive cells) or sperm cells (male reproductive cells), respectively.

Pituitary and Hypothalamus

The **pituitary** (pi-TOO-i-tair-ree) **gland** is also called the *hypophysis* (high-POF-ih-sis; *hypo,* under + *physis,* growth). It is a small gland about the size of a pea (figure 10.12, *top*). It is housed in a depression of the sphenoid bone inferior to the hypothalamus of the brain. The **hypothalamus** (high-poh-THAL-ah-muss; serves as a control center for the autonomic nervous system as well as the endocrine system. Recall from chapter 8 that the hypothalamus is a region of the diencephalon, located inferior to the thalamus. The pituitary gland lies posterior to the optic chiasm and is connected to the hypothalamus by a stalk called the **infundibulum** (IN-fun-DIB-you-lum; a funnel). The pituitary gland is divided into two parts: (1) The **anterior pituitary** is made up of epithelial cells derived from the embryonic oral cavity; (2) the **posterior pituitary** is an extension of

the brain and is composed of neurons. The hormones secreted from each lobe of the pituitary gland are listed in table 10.2.

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Figure 10.12 APR **Pituitary Gland, Its Hormones, and Their Target Tissues**

(*Top*) The pea-sized pituitary gland lies inferior to the hypothalamus of the brain. The infundibulum connects the hypothalamus and the pituitary gland. (*Bottom*) Hormones secreted by the posterior pituitary are indicated by *blue shading,* and hormones secreted by the anterior pituitary by *peach shading*.

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TABLE 10.2 Endocrine Glands, Hormones, and Their Target Tissues

Gland	Hormone	Target Tissue	Response
Pituitary gland			
Anterior	Growth hormone	Most tissues	Increases gene expression, breakdown of lipids, and release of fatty acids from cells; increases blood glucose levels
	Thyroid-stimulating hormone (TSH)	Thyroid gland	Increases thyroid hormone secretion (thyroxine and triiodothyronine)
	Adrenocorticotropic hormone (ACTH)	Adrenal cortex	Increases secretion of glucocorticoid hormones, such as cortisol; increases skin pigmentation at high concentrations
	Melanocyte-stimulating hormone (MSH)	Melanocytes in skin	Increases melanin production in melanocytes to make skin darker in color
	Luteinizing hormone (LH) or interstitial cell–stimulating hormone (ICSH)	Ovary in females, testis in males	Promotes ovulation and progesterone production in ovary; promotes testosterone synthesis and support for sperm cell production in testis

Gland	Hormone	Target Tissue	Response
	Follicle-stimulating hormone (FSH)	Follicles in ovary in females, seminiferous tubules in males	Promotes follicle maturation and estrogen secretion in ovary; promotes sperm cell production in testis
	Prolactin	Ovary and mammary gland in females, testis in males	Stimulates milk production and prolongs progesterone secretion following ovulation and during pregnancy in women; increases sensitivity to LH in males
Posterior	Antidiuretic hormone (ADH)	Kidney	Conserves water; constricts blood vessels
	Oxytocin	Uterus Mammary gland	Increases uterine contractions Increases milk letdown from mammary glands
Thyroid gland	Thyroid hormones (thyroxine, triiodothyronine)	Most cells of the body	Increase metabolic rates, essential for normal process of growth and maturation
	Calcitonin	Primarily bone	Decreases rate of bone breakdown; prevents large increase in blood Ca^{2+} levels following a meal

Gland	Hormone	Target Tissue	Response
Parathyroid glands	Parathyroid hormone	Bone, kidney	Increases rate of bone breakdown by osteoclasts; increases vitamin D synthesis, essential for maintenance of normal blood calcium levels
Adrenal medulla	Epinephrine mostly, some norepinephrine	Heart, blood vessels, liver, adipocytes	Increases cardiac output; increases blood flow to skeletal muscles and heart; increases release of glucose and fatty acids into blood; in general, prepares body for physical activity
Adrenal cortex	Mineralocorticoids(aldosterone)	Kidneys; to lesser degree, intestine and sweat glands	Increase rate of sodium transport into body; increase rate of potassium excretion; secondarily favor water retention
	Glucocorticoids (cortisol)	Most tissues (e.g., liver, fat, skeletal muscle, immune tissues)	Increase lipid and protein breakdown; increase glucose synthesis from amino acids; increase blood nutrient levels; inhibit inflammation and immune response
	Adrenal androgens	Most tissues	Insignificant in males; increase female sexual drive, growth of pubic and axillary hair

Gland	Hormone	Target Tissue	Response
Pancreas	Insulin	Especially liver, skeletal muscle, adipose tissue	Increases uptake and use of glucose and amino acids
	Glucagon	Primarily liver	Increases breakdown of glycogen and release of glucose into the circulatory system
Reproductive organs			
	Testosterone	Most tissues	Aids in sperm cell production, maintenance of functional reproductive organs, secondary sex characteristics, sexual behavior
Ovaries	Estrogens, progesterone	Most tissues	Aid in uterine and mammary gland development and function, external genitalia structure, secondary sex characteristics, sexual behavior, menstrual cycle
Uterus, ovaries, inflamed tissues	Prostaglandins	Most tissues	Mediate inflammatory responses; increase uterine contractions and ovulation
Thymus	Thymosin	Immune tissues	Promotes immune system development and function
Pineal gland	Melatonin	Among others, hypothalamus	Inhibits secretion of gonadotropin-releasing hormone, thereby inhibiting reproduction

Hormones from the pituitary gland control the functions of many other glands in the body, such as the ovaries, the testes, the thyroid gland, and the adrenal cortex (figure 10.12, *bottom*). The pituitary gland also secretes hormones that influence growth, kidney function, birth, and milk production by the mammary glands. Historically, the pituitary gland was known as the body's *master gland* because it controls the function of so many other glands. However, we now know that the hypothalamus controls the pituitary gland in two ways: (1) hormonal control and (2) direct innervation.

Hypothalamic Control of the Anterior Pituitary

The anterior pituitary gland synthesizes hormones, whose secretion is under the control of the hypothalamus. Figure 10.13 outlines the relationship between the hypothalamus and the anterior pituitary.

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PROCESS Figure

PROCESS Figure 10.13 APR **Hypothalamus and Anterior Pituitary**

Secretion of hormones from the anterior pituitary is regulated by releasing and inhibiting hormones from the hypothalamus.

Given that the anterior pituitary releases multiple hormones, how is it that a particular hypothalamus-releasing hormone stimulates the secretion of a specific anterior pituitary hormone?

❶ Neurons of the hypothalamus produce neuropeptides and secrete them into a capillary bed in the hypothalamus. Stimuli within the nervous system regulate the secretion of releasing hormones and inhibiting hormones (*circles*) from neurons of the hypothalamus.

❷ Releasing hormones and inhibiting hormones pass through the hypothalamohypophysial portal system to the anterior pituitary.

❸ Once the neuropeptides arrive at the anterior pituitary gland, they leave the blood and bind to membrane-bound receptors involved with regulating anterior pituitary hormone secretion. The capillary beds and veins that transport the releasing and inhibiting hormones are called the **hypothalamic-pituitary portal system.** The hypothalamic neuropeptides function as either releasing hormones or inhibiting hormones. Each releasing hormone stimulates the production and secretion of a specific hormone by the anterior pituitary. Each inhibiting hormone reduces the production and secretion of a specific hormone by the anterior pituitary.

❹ In response to releasing hormones, anterior pituitary hormones (*squares*) travel in the blood to their target tissue, which in some cases, are other endocrine glands.

Hypothalamic Control of the Posterior Pituitary

The posterior pituitary is a storage location for two hormones synthesized by special neurons in the hypothalamus. Figure 10.14 outlines the relationship between the hypothalamus and the posterior pituitary.

PROCESS Figure

PROCESS Figure 10.14 APR **Hypothalamus and Posterior Pituitary**

Secretion of hormones from the posterior pituitary is regulated by neural input.

Are the posterior pituitary hormones water-soluble or lipid-soluble hormones? How do you know, based solely on their mode of storage?

❶ Stimulation of neurons within the hypothalamus controls the secretion of the posterior pituitary hormones.

❷ Action potentials are conducted by axons of the hypothalamic neurons through the hypothalamohypophysial tract to the posterior pituitary. The axon endings of neurons store hormones in the posterior pituitary.

❸ In the posterior pituitary gland, action potentials cause the release of hormones (*circles*) from axon terminals into the circulatory system.

❹ The hormones pass through the circulatory system and influence the activity of their target tissues.

Within the hypothalamus and pituitary, the nervous and endocrine systems are closely interrelated. Emotions such as joy and anger, as well as chronic stress,

influence the endocrine system through the hypothalamus. Conversely, hormones of the endocrine system can influence the functions of the hypothalamus and other parts of the brain.

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Hormones of the Anterior Pituitary

The anterior pituitary is regulated differently than the posterior pituitary because its hormones are synthesized by cells in the anterior pituitary.

The hormones secreted from the anterior pituitary are proteins. They are transported in the blood, have a life span measured in minutes, and bind to membrane-bound receptors on their target cells. For the most part, each hormone is secreted by a separate cell type.

Many hormones from the anterior pituitary gland are tropic hormones, which stimulate the secretion of other hormones from the target tissues (see figure 10.5).

Growth Hormone

Growth hormone (GH) stimulates the growth of bones, muscles, and other organs by increasing gene expression. It also slows protein breakdown during periods of food deprivation and favors lipid breakdown.

Too little growth hormone secretion can result from abnormal development of the pituitary gland. A young person suffering from a deficiency of growth hormone remains small, although normally proportioned, and is called a **pituitary dwarf** (dwawrf). This condition can be treated by administering growth hormone. Because GH is a protein, it is difficult to produce artificially using conventional techniques. However, human genes for GH have been successfully introduced into bacteria using genetic engineering techniques. The gene in the bacteria causes GH synthesis, and the GH can be extracted from the medium in which the bacteria are grown. Thus, modern genetic engineering has provided a source of human GH for people who produce inadequate quantities.

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Excess growth hormone secretion can result from hormone-secreting tumors of the pituitary gland. If excess growth hormone is present before bones finish growing in length, exaggerated bone growth occurs. The person becomes abnormally tall, a condition called **giantism** (JYE-an-tizm). If excess hormone is secreted after growth in bone length is complete, growth continues in bone diameter only. As a result, the facial features and hands become abnormally large, a condition called **acromegaly** (ak-roh-MEG-ah-lee).

The secretion of growth hormone is controlled by two hormones from the hypothalamus. A releasing hormone stimulates growth hormone secretion, and an

inhibiting hormone inhibits its secretion. Most people have a rhythm of growth hormone secretion, with daily peak levels occurring during deep sleep. Growth hormone secretion also increases during periods of fasting and exercise. Blood levels of growth hormone do not become significantly elevated during periods of rapid growth, although children tend to have somewhat higher blood levels of growth hormone than do adults. In addition to growth hormone, genetics, nutrition, and reproductive hormones influence growth.

Part of the effect of growth hormone is influenced by a group of protein hormones called **insulin-like growth factors (IGFs),** or *somatomedins* (SOH-mah-toh-MEE-dins). Growth hormone increases IGF secretion from tissues such as the liver, and the IGF molecules bind to receptors on the cells of tissues such as bone and cartilage, where they stimulate growth. The IGFs are similar in structure to insulin and can bind, to some degree, to insulin receptors. Also, insulin, at high concentrations, can bind to IGF receptors.

Apply It 2

Zach has a son who wants to be a basketball player. Zach knows something about GH. He asked his son's doctor if he would prescribe some GH for his son, so that he can grow taller. What do you think the doctor tells Zach? Why?

Thyroid-Stimulating Hormone

Thyroid-stimulating hormone (TSH) binds to membrane-bound receptors on cells of the thyroid gland and stimulates the secretion of thyroid hormone. TSH can also stimulate growth of the thyroid gland. Thus, when too much TSH is secreted, the thyroid gland enlarges and secretes too much thyroid hormone. When too little TSH is secreted, the thyroid gland decreases in size and secretes too little thyroid hormone. The rate of TSH secretion is regulated by a releasing hormone from the hypothalamus.

Adrenocorticotropic Hormone

Adrenocorticotropic (ah-DREE-noh-KOR-tih-koh-TROH-pik) **hormone (ACTH)** binds to membrane-bound receptors on cells of the adrenal cortex. ACTH increases the secretion of a hormone from the adrenal cortex called **cortisol** (KOR-tih-sol), also called hydrocortisone. ACTH is required to keep the adrenal cortex from degenerating. ACTH molecules also bind to melanocytes in the skin and increase skin pigmentation (see chapter 5). One symptom of too much ACTH secretion is darkening of the skin. The rate of ACTH secretion is increased by a releasing hormone from the hypothalamus.

Gonadotropins

Gonadotropins (GOH-nad-oh-TROH-pins) bind to membrane-bound receptors on the cells of the gonads (ovaries and testes). The gonadotropins regulate the growth, development, and functions of the gonads. The two major gonadotropins are (1) **luteinizing** (LOO-tee-in-eye-zing) **hormone (LH)** and (2) **follicle-stimulating hormone (FSH).** In females, LH stimulates ovulation. LH also promotes the secretion of the reproductive hormones, estrogen and progesterone, from the ovaries. In males, LH stimulates interstitial cells of the testes to secrete the reproductive hormone testosterone and FSH stimulates the development of follicles in the ovaries and sperm cells in the testes. Without LH and FSH, the ovaries and testes decrease in size, no longer produce oocytes or sperm cells, and no longer secrete hormones. A single releasing hormone from the hypothalamus increases the secretion of both LH and FSH.

MICROBES IN YOUR BODY

Hormonal Regulation of Nutrient Metabolism is Influenced by Gut Microbes

Obesity has increased at an alarming rate over the last three decades. It is estimated that over 150 billion adults worldwide are overweight or obese. In the United States, 40% of adults are obese. As obesity rates have increased, so have the rates of obesity-related health conditions such as insulin resistance, diabetes, and cardiovascular disease. Why this dramatic increase? There are two main reasons for obesity: diet/lifestyle and gut bacteria; it seems these two may be related.

The most familiar cause of obesity is diet and lifestyle. The "typical" Western diet consists of frequent large meals high in refined grains, red meat, saturated fats, and sugary drinks. Combined with a reduction in physical activity and less sleep for many Americans, the Western diet and lifestyle can lead to obesity and poor health.

However, could humans' gut microbiota be just as responsible (or even more responsible) for obesity? Comparisons between the gut microbiota of lean versus obese individuals seem to suggest the possibility of an important link between gut microbiota and our weight. The human gut, like other animals, is densely populated with microbiota. The majority (90%) of human gut bacteria fall into two groups: Firmicutes and Bacteroidetes. Lean people have more Bacteroidetes than Firmicutes, while the opposite is true for obese people.

We now know that gut microbiota affect nutrient processing and absorption, hormonal regulation of nutrient use by body cells, and even our hunger level.

Changes in gut microbiota alter the hormonal regulation of nutrient use. Inflammation-promoting effects of an imbalanced gut microbiota is thought to induce obesity via promoting insulin resistance, a known autoimmune malfunction. Normal gut microbiota metabolism is critical for secretion of several anti-hunger hormones, and anti-depressive neurotransmitters and neurochemicals. Shifts in normal gut microbiota, as related to diet, may very well disrupt normal anti-hunger signals and gut permeability, leading to over-eating and inflammation related to obesity.

Can gut microbiota in obese people be manipulated to cause them to become lean? Several possibilities exist, including the distinct possibility that prescribing antibiotics against bacteria associated with obesity could shift the metabolism of an obese person to become leaner.

Another possibility is the use of prebiotics— nondigestible sugars that enhance the growth of beneficial microbiota. Finally, probiotic use is another possible intervention for obesity. Probiotics are nonpathogenic live bacteria that confer a health benefit to the host. This is a rapidly expanding field that holds much promise, but it is still in its beginning stages of our understanding.

Prolactin

Prolactin (proh-LAK-tin; *pro,* precursor + *lact,* milk) binds to membrane-bound receptors in cells of the breast, where it helps promote development of the breast during pregnancy and stimulates the production of milk following pregnancy. The regulation of prolactin secretion is complex and may involve several substances released from the hypothalamus. However, the principal control is exerted by dopamine, formerly called prolactin-inhibiting hormone. Prolactin is now thought to play many roles in homeostasis, including regulation of the ion composition of blood and immune function.

Melanocyte-Stimulating Hormone

Melanocyte-stimulating (MEL-an-oh-cyte) **hormone (MSH)** binds to membrane-bound receptors on melanocytes and causes them to synthesize melanin. The structure of MSH is similar to that of ACTH, and oversecretion of either hormone causes the skin to darken. Regulation of MSH is not well understood, but there appear to be two regulatory hormones from the hypothalamus—one that increases MSH secretion and one that decreases it.

Hormones of the Posterior Pituitary

Antidiuretic Hormone

Antidiuretic (an-tee-die-you-RET-ik; *anti,* against + *uresis,* urine volume) **hormone (ADH)** binds to membrane-bound receptors and increases water reabsorption by kidney tubules. This results in less water lost as urine. ADH can also cause blood vessels to constrict when released in large amounts. Consequently, ADH is also called *vasopressin* (vay-soh-PRESS-in). Reduced ADH release from the posterior pituitary results in large amounts of dilute urine.

A lack of ADH secretion causes diabetes insipidus, which is the production of a large amount of dilute urine. The consequences of diabetes insipidus are not obvious until the condition becomes severe, producing many liters of urine each day. The large urine volume is created by excess water loss from the blood, which increases the concentration of the body fluids and causes the loss of important electrolytes, such as Ca^{2+}, Na^{+}, and K^{+}. The lack of ADH secretion may be familiar to some who have ever had alcohol to drink. The diuretic actions of alcohol are due to its inhibition of ADH secretion.

Oxytocin

Oxytocin (OK-see-TOH-sin; swift birth) binds to membrane-bound receptors and causes contraction of the smooth muscle cells of the uterus as well as milk letdown from the breasts in lactating women. Commercial preparations of oxytocin, known as Pitocin, are given under certain conditions to assist in childbirth and to constrict uterine blood vessels following childbirth.

Thyroid Gland

The **thyroid** (THIGH-royd; shield-shaped) **gland** synthesizes and secretes three hormones: (1) triiodothyronine (T_3), (2) thyroxine (tetraiodothyronine; T_4), and (3) calcitonin. It is made up of two lobes connected by a narrow band called the **isthmus** (IS-muhs; a constriction). The lobes are located on each side of the trachea, just inferior to the larynx (figure 10.15*a,b*). The thyroid gland is one of the largest endocrine glands. It appears more red than the surrounding tissues because it is highly vascular. It is surrounded by a connective tissue capsule.

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Figure 10.15 APR **Thyroid and Parathyroid Glands**

(*a*) Anterior view of the thyroid gland. (*b*) The four small parathyroid glands are embedded in the posterior surface of the thyroid gland. (*c*) Three-dimensional interpretive drawing of thyroid follicles and parafollicular cells. (*d*) Light micrograph

of thyroid and parathyroid tissue.
(d) ©Victor Eroschenko

The thyroid gland contains numerous **thyroid follicles,** which are small spheres with walls composed of simple cuboidal epithelium (figure 10.15*c,d*). The epithelial cells of the follicles synthesize the thyroid hormones, T_3 and T_4, which are stored within the follicles. Each thyroid follicle is filled with the protein thyroglobulin (thigh-roh-GLOB-you-lin), to which thyroid hormones are attached. Thyroid hormones attach to nuclear receptors in their target cells and regulate the metabolic rate of the body (table 10.2). Between the follicles is a network of loose connective tissue that contains capillaries and scattered **parafollicular cells,** or C cells, which secrete the hormone **calcitonin.**

The thyroid gland requires iodine to synthesize thyroid hormones. **Thyroxine** (thigh-ROK-seen) or *tetraiodothyronine* (TET-rah-eye-oh-doh-THIGH-roh-neen). contains four iodine atoms and is abbreviated T_4. **Triiodothyronine** (trie-EYE-oh-doh-THIE-roh-neen), contains three iodine atoms and is abbreviated T_3. Without iodine, thyroid hormones are neither produced nor secreted. A deficiency of iodine is not as common in the United States as it once was. Table salt with iodine added to it (iodized salt) is available in grocery stores, and vegetables grown in soil rich in iodine can be shipped to most places.

Thyroid hormone secretion is regulated by hormones from both the hypothalamus and pituitary. Figure 10.16 details the steps in the regulation of thyroid hormone secretion.

Pituitary
Thyroid

1 TRH is secreted
Anterior pituitary (adenohypophysis)
Posterior pituitary (neurohypophysis)
5 T_3 and T_4 exert negative feedback
2 TSH is secreted
TSH
Thyroid
Water-soluble hormone (TSHcvv)
Membrane-bound receptor
G protein complex
ATP
Adenylate cyclase
cAMP
Protein kinase

Figure 10.16 **Regulation of Thyroid Hormone (T_3 and T_4) Secretion**

Thyroid hormones are regulated by the hypothalamus and anterior pituitary.

1. The hypothalamus secretes TSH-releasing hormone, also known as TRH. Stress and hypothermia cause TRH to be released from neurons within the hypothalamus. It passes through the hypothalamohypophysial portal system to the anterior pituitary.
2. TRH travels to the anterior pituitary to stimulate the secretion of thyroid-stimulating hormone (TSH).
3. TSH causes increased synthesis and release of T_3 and T_4 into the general circulation. Small fluctuations in blood TSH levels occur on a daily basis, with a small increase at night. Increasing blood levels of TSH increase the synthesis and release of thyroid hormones from thyroglobulin. Decreasing blood levels of TSH decrease the synthesis and release of thyroid hormones.
4. T_3 and T_4 act on target tissues to produce a response.
5. T_3 and T_4 also have an inhibitory effect on the secretion of TRH from the hypothalamus and TSH from the anterior pituitary.

The negative-feedback effect of thyroid hormones on the hypothalamus and pituitary results in increasing levels of thyroid hormones inhibiting the secretion of TSH-releasing hormone from the hypothalamus and inhibiting TSH secretion from the anterior pituitary gland. Decreasing thyroid hormone levels allow additional TSH-releasing hormone and TSH to be secreted. Because of the

negative-feedback effect, the thyroid hormones fluctuate within a narrow concentration range in the blood. However, a loss of negative feedback will result in excess TSH. This causes the thyroid gland to enlarge, a condition called a **goiter** (GOY-ter). One type of goiter develops if iodine in the diet is too low. As less thyroid hormone is synthesized and secreted, TSH-releasing hormone and TSH secretion increase above normal levels and cause dramatic enlargement of the thyroid gland.

Because thyroid hormones are critical regulators of growth and development, failure to maintain appropriate levels of thyroid hormones dramatically affects the body's functions. A lack of thyroid hormones is called **hypothyroidism** (high-poh-THIGH-royd-ism). In infants, hypothyroidism can result in **cretinism** (KREH-tin-ism). Cretinism is characterized by developmental delay, short stature, and abnormally formed skeletal structures. In adults, the lack of thyroid hormones results in a decreased metabolic rate, which can result in low body temperature, weight gain, reduced appetite, and lethargy, among other symptoms.

An elevated rate of thyroid hormone secretion is **hyperthyroidism** (high-per-THIGH-royd-ism). Hyperthyroidism causes an increased metabolic rate, extreme nervousness, and chronic fatigue. **Graves disease** is an autoimmune disease that causes hyperthyroidism. This disease occurs when the immune system produces abnormal proteins that are similar in structure and function to TSH, which overstimulates the thyroid gland. Graves disease is often accompanied by bulging of the eyes, a condition called **exophthalmia** (ek-sof-THAL-me-ah) (see Systems Pathology, "Graves Disease").

Apply It 3

In people with Graves disease (hyperthyroidism), the immune system produces a large amount of a protein that is so much like TSH that it binds to cells of the thyroid gland and acts like TSH. Unlike TSH, however, the secretion of this protein does not respond to negative feedback. Explain the effect of this abnormal protein on the structure and function of the thyroid gland and the release of hormones from the hypothalamus and anterior pituitary gland.

In addition to secreting thyroid hormones, the parafollicular cells of the thyroid gland secrete a hormone called calcitonin (see figure 10.15*c*). Calcitonin is secreted if the blood concentration of Ca^{2+} becomes too high. Calcitonin lowers blood Ca^{2+} levels to return to their normal range (figure 10.17). Calcitonin binds to membrane-bound receptors of osteoclasts and inhibits them. Inhibition of osteoclasts reduces the rate of Ca^{2+} reabsorption (breakdown) from bone. Calcitonin may prevent blood Ca^{2+} levels from becoming overly elevated following a meal that contains a high concentration of Ca^{2+}.

Homeostasis Figure 10.17 **Regulation of Calcium Ion Blood Levels**

(1) Blood Ca^{2+} is within its normal range. (2) Blood Ca^{2+} level increases outside the normal range. (3) The parafollicular cells and the parathyroid gland cells detect elevated blood Ca^{2+}. The parafollicular cells secrete calcitonin; the parathyroid gland cells decrease PTH secretion. (4) There is less bone reabsorption and less uptake of Ca^{2+} from both the kidney and the intestine. (5) Blood Ca^{2+} level drops back to its normal range. (6) Homeostasis is restored. Observe the response to a drop in blood Ca^{2+} by following the *red arrows*.

Calcitonin helps prevent elevated blood Ca^{2+} levels, but a lack of calcitonin secretion does not result in a prolonged increase in those levels. Other mechanisms controlling blood Ca^{2+} levels compensate for the lack of calcitonin secretion.

Parathyroid Glands

Four tiny **parathyroid** (pair-ah-THIGH-royd) **glands** are embedded in the posterior wall of the thyroid gland (see figure 10.15*b*, *d*). The parathyroid glands secrete a hormone called **parathyroid hormone (PTH),** which is essential for the regulation of blood calcium levels (table 10.2). In fact, PTH is more important than calcitonin in regulating blood Ca^{2+} levels. PTH has many effects:

1. PTH increases active vitamin D formation through effects on membrane-bound receptors of renal tubule cells in the kidneys. Vitamin D stimulates increased Ca^{2+} absorption by intestinal epithelial cells.
2. PTH secretion increases blood Ca^{2+} levels. PTH binds to receptors on osteoblasts. In turn, osteoblasts secrete substances that stimulate osteoclasts to reabsorb bone.
3. PTH decreases loss of Ca^{2+} in the urine.

Vitamin D is produced from precursors in the skin that are modified by the liver and kidneys. Ultraviolet light acting on the skin is required for the first stage of vitamin D synthesis, and the final stage of synthesis in the kidney is stimulated by PTH. Vitamin D can also be supplied in the diet.

Understand

Apply It 4

Explain why a person who stays indoors all day and lacks vitamin D has bones that are softer than normal.

Decreasing blood Ca^{2+} levels stimulate an increase in PTH secretion (figure 10.17). For example, if too little Ca^{2+} is consumed in the diet or if a person suffers from a prolonged lack of vitamin D, blood Ca^{2+} levels decrease, and PTH secretion increases. The increased PTH increases the rate of bone reabsorption. Blood Ca^{2+} levels can be maintained within a normal range, but prolonged reabsorption of bone results in reduced bone density, as manifested by soft, flexible bones that are easily deformed in young people and porous, fragile bones in older people.

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Increasing blood Ca^{2+} levels cause a decrease in PTH secretion (figure 10.17). The decreased PTH secretion leads to reduced blood Ca^{2+} levels. In addition, increasing blood Ca^{2+} levels stimulate calcitonin secretion, which also causes blood Ca^{2+} levels to decline.

An abnormally high rate of PTH secretion is called **hyperparathyroidism.** One cause is a tumor in a parathyroid gland. The elevated blood levels of PTH increase bone reabsorption, which elevates blood Ca^{2+} levels. As a result, bones can become soft, deformed, and easily fractured. In addition, the elevated blood

Ca^{2+} levels make nerve and muscle cells less excitable, resulting in fatigue and muscle weakness. The excess Ca^{2+} can be deposited in soft tissues of the body, causing inflammation. In addition, kidney stones can result.

An abnormally low rate of PTH secretion is called **hypoparathyroidism.** Hypoparathyroidism can result from injury to or the surgical removal of the thyroid and parathyroid glands. The low blood levels of PTH lead to reductions in the rate of bone reabsorption and the formation of vitamin D. As a result, blood Ca^{2+} levels decrease. In response to low blood Ca^{2+} levels, nerves and muscles become excitable and produce spontaneous action potentials that cause frequent muscle cramps or tetanus. Severe tetanus can affect the respiratory muscles; breathing stops, resulting in death.

Adrenal Glands

The **adrenal** (ah-DREE-nal; near or on the kidneys) **glands** are two small glands located superior to each kidney (figure 10.18*a*; table 10.2). Each adrenal gland has an inner part, called the **adrenal medulla** (marrow, or middle), and an outer part, called the **adrenal cortex** (bark, or outer). The adrenal medulla and the adrenal cortex function as separate endocrine glands.

Figure 10.18 APR **Anatomy and Histology of the Adrenal Gland**

(*a*) An adrenal gland lies at the superior pole of each kidney. (*b*) The adrenal glands have an outer cortex and an inner medulla. (*c*) The cortex is surrounded by a connective tissue capsule.

(c) ©Victor Eroschenko

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Adrenal Medulla

The adrenal medulla secretes two major hormones: (1) **epinephrine** (ep-ih-NEF-rin; *epi,* upon + *nephros,* kidney; *adrenaline* (ah-DREN-ah-lin)), which accounts for 80% of the adrenal medulla secretions and (2) **norepinephrine,** (NOR-ep-ih-NEF-rin) which accounts for 20%. Figure 10.19 illustrates the mechanism by which the adrenal medulla secretes its hormones.

PROCESS Figure

PROCESS Figure 10.19 APR **Regulation of Adrenal Medullary Secretions**

Stimulation of the hypothalamus by stress, physical activity, or low blood glucose levels causes action potentials to travel through the sympathetic nervous system to the adrenal medulla. In response, the adrenal medulla releases epinephrine and smaller amounts of norepinephrine into the blood. These hormones have several effects that prepare the body for physical activity.

How do epinephrine and norepinephrine from the adrenal medulla differ in their delivery to their targets from epinephrine and norepinephrine released by neurons of the sympathetic nervous system?

❶ Secretion of adrenal medulla hormones can occur under various conditions that activate the sympathetic nervous system. For example, stress, low blood glucose, or excitement cause secretion of these hormones.

❷ An increased frequency of action potentials conducted through the sympathetic division of the autonomic nervous system stimulates the adrenal medulla to secrete epinephrine and some norepinephrine into the circulatory system.

❸ These hormones bind to membrane-bound receptors in their target tissues, where they prepare the body for intense physical activity.

Epinephrine and norepinephrine are called the **fight-or-flight** hormones. They prepare the body for intense physical activity. The major effects of the hormones released from the adrenal medulla are

1. Release of stored energy sources to support increased physical activity. For example, glucose derived from breakdown of liver glycogen and fatty acids derived from the breakdown of adipose tissue.
2. Increased blood pressure. Two effects of epinephrine cause an elevated blood pressure.
   a. Increased heart rate.
   b. Constriction of blood vessels in skin and internal organs.
3. Increased blood flow to skeletal muscle. The vasoconstriction in the internal organs and skin blood vessels reduces blood flow to those tissues. The smooth muscle in skeletal muscle blood vessels does not contract. That, in combination with decreased blood flow elsewhere, explains the increased blood flow to the skeletal muscle.
4. Increased metabolic rate of several tissues, especially skeletal muscle, cardiac muscle, and nervous tissue.

Responses to hormones from the adrenal medulla reinforce the effect of the sympathetic division of the autonomic nervous system. Thus, the adrenal medulla and the sympathetic division function together to prepare the body for physical activity and to produce the fight-or-flight response and many other responses to stress.

Adrenal Cortex

The adrenal cortex secretes three classes of steroid hormones: (1) mineralocorticoids (MIN-er-al-oh-KOHR-ti-koydz), (2) glucocorticoids (gloo-koh-KOR-ti-koids), and (3) adrenal androgens (AN-droh-jens). The molecules of all three classes of steroid hormones enter their target cells and bind to nuclear receptor molecules. However, the hormones and the receptors of each class have unique structural and functional characteristics.

As their name suggests, the mineralocorticoids regulate ion balance in the blood. The mineralocorticoids are the major secretory products of the zona glomerulosa of the adrenal cortex. **Aldosterone** (al-DOS-ter-ohn) is produced in the greatest amounts, although other, closely related mineralocorticoids are also secreted. Aldosterone is secreted under low blood pressure conditions. It returns blood pressure to its normal range through modulation of kidney function. Aldosterone increases the rate of Na^+ reabsorption by the kidneys, which increases blood levels of Na^+. The higher blood Na^+ levels enhance water reabsorption through osmosis. Recall from chapter 3 that osmosis is the diffusion of water toward higher solute areas. This reabsorption of water increases blood volume and thereby increases blood pressure. Aldosterone also stimulates K^+ excretion into the urine by the kidneys, which lowers blood levels of K^+. In addition, aldosterone increases the rate of H^+ excretion into the urine. When aldosterone is secreted in

high concentrations, reduced blood K^+ levels and alkalosis (elevated pH of body fluids) may result. The specific effects of aldosterone and the mechanisms controlling aldosterone secretion are discussed along with cardiovascular system functions in chapter 13 and with kidney functions in chapter 18.

Apply It 5

Explain the effects of reduced aldosterone secretion on blood levels of Na^+ and K^+, as well as on blood pressure.

Glucocorticoids help to provide energy for cells by stimulating the increased use of lipids and proteins. It is the middle layer of the adrenal cortex that secretes the **glucocorticoid hormones,** primarily **cortisol** (KOR-tih-sol). The responses are classified as metabolic, developmental, or anti-inflammatory. Glucocorticoids cause lipid breakdown, reduce glucose and amino acid uptake in skeletal muscle, stimulate synthesis of new glucose from precursor molecules, such as amino acid, and increase protein degradation. Glucocorticoids also increase blood glucose levels and glycogen deposits in cells. The glucose and glycogen are a reservoir of molecules that can be metabolized rapidly.

Glucocorticoids decrease the intensity of the inflammatory and immune responses by decreasing both the number of white blood cells and the secretion of inflammatory chemicals from tissues. Synthetic glucocorticoids are often used to suppress the immune response in people suffering from autoimmune conditions and in transplant recipients (see chapter 14). The anti-inflammatory effect of cortisol is important under conditions of stress, when the rate of glucocorticoid secretion is relatively high. Although the ability to respond to stress is adaptive for short periods of time, responses triggered by stressful conditions are harmful if they occur for long periods. Prolonged stress can lead to hypertension (elevated blood pressure), heart disease, ulcers, inhibited immune system function, changes in mood, and other conditions. Humans are frequently exposed to prolonged psychological stress from high-pressure jobs, the inability to meet monetary obligations, or social expectations. Although responses to stress prepare a person for physical activity, increased physical activity is often not an appropriate response to the situation causing the stress. Long-term exposure to stress under conditions in which physical activity and emotions must be constrained may be harmful. Techniques that effectively reduce responses to stressful conditions, such as biofeedback, meditation, or other relaxation exercises, can be helpful to people who are exposed to chronic stress.

The regulation of cortisol secretion is outlined in figure 10.20.

PROCESS Figure

PROCESS Figure 10.20 APR **Regulation of Cortisol Secretion from the Adrenal Cortex**

Cortisol secretion is stimulated by the anterior pituitary hormone, ACTH.

Understand ***Explain why the drug cortisone (KOR-tih-sohn), a steroid closely related to cortisol, is prescribed to treat joint injuries, allergies, or asthma.***

❶ Corticotropin-releasing hormone (CRH) is released from hypothalamic neurons in response to stress or low blood glucose, and passes, by way of the hypothalamohypophysial portal system, to the anterior pituitary.

❷ In the anterior pituitary, CRH binds to and stimulates cells that secrete adrenocorticotropic hormone (ACTH).

❸ The middle layer of the adrenal cortex is very sensitive to ACTH. Once ACTH binds to its membrane-bound receptors, the adrenal cortex increases cortisol secretion.

❹ Cortisol acts on target tissues, resulting in increased breakdown of lipids and proteins, higher glucose levels, and increased anti-inflammatory effects.

❺ Both ACTH and cortisol act via negative feedback to inhibit CRH secretion from the hypothalamus.

High concentrations of cortisol in the blood inhibit ACTH secretion from the anterior pituitary, and low concentrations stimulate it. This negative-feedback loop is important in maintaining blood cortisol levels within a controlled range of concentration. Stress and hypoglycemia (low levels of glucose in the blood) trigger a large increase in CRH release from the hypothalamus by causing a rapid increase in blood levels of cortisol. In addition, CRH levels vary significantly throughout the day.

Apply It 6

Cortisone is sometimes given to people who have severe allergies or extensive inflammation or to people who suffer from autoimmune diseases. Taking this substance for long periods of time can damage the adrenal cortex. Explain how this damage can occur.

The third class of hormones, secreted by the inner layer of the adrenal cortex, is composed of the **adrenal androgens,** which stimulate the development of male secondary sex characteristics. Small amounts of androgens are secreted from the adrenal cortex in both males and females. In adult males, most androgens are secreted by the testes. In adult females, the adrenal androgens influence the female sex drive. If the secretion of reproductive hormones from the adrenal cortex is abnormally high, exaggerated male characteristics develop in both males and females. This condition is most apparent in females and in males before puberty, when the effects are not masked by the secretion of androgens by the testes.

Pancreas, Insulin, and Diabetes

The endocrine part of the **pancreas** (PAN-kree-as) consists of **pancreatic islets** (islets of Langerhans), which are dispersed throughout the exocrine portion of the pancreas (figure 10.21). The islets consist of three cell types, each of which secretes a separate hormone. (1) **Alpha cells** secrete glucagon, (2) **beta cells** secrete insulin, and (3) **delta cells** secrete somatostatin. These three hormones regulate the blood levels of nutrients, especially glucose (table 10.3).

Figure 10.21 APR **Structure of the Pancreas**

The endocrine portion of the pancreas is made up of scattered pancreatic islets. Alpha cells secrete glucagon, beta cells secrete insulin, and delta cells secrete somatostatin. The exocrine portion of the pancreas surrounds the pancreatic islets and produces digestive enzymes that are carried through a system of ducts to the small intestine. The stain used for the light micrograph does not distinguish between alpha, beta, and delta cells.

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TABLE 10.3 Effects of Insulin and Glucagon on Target Tissues

Target Tissue	Insulin Responses	Glucagon Responses
Skeletal muscle, cardiac muscle, cartilage, bone fibroblasts, blood cells, mammary glands	Increases glucose uptake and glycogen synthesis; increases uptake of amino acids	Has little effect
Liver	Increases glycogen synthesis; increases use of glucose for energy	Causes rapid increase in the breakdown of glycogen to glucose and release of glucose into the blood; increases the formation of glucose from amino acids and, to some degree, from lipids; increases metabolism of fatty acids
Adipose cells	Increases glucose uptake, glycogen synthesis, lipid synthesis	High concentrations cause breakdown of lipids; probably unimportant under most conditions

Target Tissue	Insulin Responses	Glucagon Responses
Nervous system	Has little effect except to increase glucose uptake in the satiety center	Has no effect

It is very important to maintain blood glucose levels within a normal range (figure 10.22). A below-normal blood glucose level causes the nervous system to malfunction because glucose is the nervous system's main source of energy. When blood glucose decreases, other tissues rapidly break down lipids and proteins to provide an alternative energy source. As lipids are broken down, the liver converts some of the fatty acids to acidic **ketones** (KEE-tonez), which are released into the blood. When blood glucose levels are very low, the breakdown of lipids can cause the release of enough fatty acids and ketones to reduce the pH of the body fluids below normal, a condition called **acidosis** (as-ih-DOH-sis). The amino acids of proteins are broken down and used by the liver to synthesize glucose.

Homeostasis Figure 10.22 **Regulation of Blood Glucose Levels**

(1) Blood glucose is within its normal range. (2) Blood glucose level increases outside the normal range. (3) The pancreatic islets secrete insulin in direct response to elevated blood glucose. (4) Most tissues take up glucose when insulin binds to its receptor on the tissues. (5) Blood glucose level drops back to its normal range. (6) Homeostasis is restored. Observe the response to a drop in blood glucose by following the *red arrows*.

Elevated blood glucose levels stimulate beta cells to secrete **insulin** (IN-syu-lin). Additionally, increased parasympathetic stimulation associated with digestion of a meal stimulates insulin secretion. Increased blood levels of certain amino acids also stimulate insulin secretion. There are two signals that inhibit insulin secretion: (1) low blood glucose levels and (2) stimulation of the sympathetic nervous system. The decrease in insulin levels allows blood glucose to be conserved to provide the brain with adequate glucose and to allow other tissues to metabolize fatty acids and glycogen stored in the cells.

The major target tissues for insulin are the liver, adipose tissue, muscles, and the area of the hypothalamus that controls appetite, called the **satiety** (sa-TIE-eh-tee; fulfillment of hunger) **center.** Insulin binds to membrane-bound receptors and, either directly or indirectly, increases the rate of glucose and amino acid uptake in these tissues. Glucose is converted to glycogen or lipids, and the amino acids are used to synthesize protein. The effects of insulin on target tissues are summarized in table 10.3.

Diabetes mellitus (die-ah-BEE-teez MEL-ih-tus; much urine + honey or sweetened) is the body's inability to regulate blood glucose levels within the normal range. There are two types of diabetes mellitus, type 1 and type 2. Type 1 diabetes mellitus occurs when too little insulin is secreted from the pancreas. Type 2 diabetes mellitus is caused by either too few insulin receptors on target cells or defective receptors on target cells. The defective receptors do not respond normally to insulin.

In type 1 diabetes mellitus, tissues cannot take up glucose effectively, causing blood glucose levels to become very high, a condition called **hyperglycemia** (HIGH-per-glye-SEE-mee-ah; *hyper,* above + *glycemia,* blood glucose). Because glucose cannot enter the cells of the satiety center in the brain without insulin, the satiety center responds as if there were very little blood glucose, resulting in an exaggerated appetite. The excess glucose in the blood is excreted in the urine, making the urine volume much greater than normal. Because of excessive urine production, the person has a tendency to become dehydrated and thirsty. Even though blood glucose levels are high, lipids and proteins are broken down to provide an energy source for metabolism, resulting in the wasting away of body tissues, acidosis, and ketosis. People with this condition also exhibit a lack of energy. Insulin must be injected regularly to adequately control blood glucose levels. When too much insulin is present, as occurs when a diabetic is injected with too much insulin or has not eaten after an insulin injection, blood glucose levels become very low. The brain, which depends primarily on glucose for an energy source, malfunctions. This condition, called insulin shock, can cause disorientation and convulsions and may result in loss of consciousness. Fortunately genetic engineering has allowed synthetic insulin to become widely available to diabetics.

Glucagon (GLUE-kah-gon) is released from the alpha cells when blood glucose levels are low. Glucagon binds to membrane-bound receptors primarily in the liver, causing the glycogen stored in the liver to be converted to glucose. The glucose is then released into the blood to increase blood glucose levels. After a meal, when blood glucose levels are elevated, glucagon secretion is reduced.

Somatostatin (SOH-mah-TOH-stat-in) is released by the delta cells in response to food intake. Somatostatin inhibits the secretion of insulin and glucagon and inhibits gastric tract activity.

Apply It 7

How are the rates of insulin and glucagon secretion affected immediately following a large meal rich in carbohydrates? How are they affected after 12 hours without eating?

Insulin and glucagon together regulate blood glucose levels (see figure 10.22). When blood glucose levels increase, insulin secretion increases, and glucagon secretion decreases. When blood glucose levels decrease, the rate of insulin secretion declines, and the rate of glucagon secretion increases. Other hormones, such as epinephrine, cortisol, and growth hormone, also maintain blood levels of nutrients. When blood glucose levels decrease, these hormones are secreted at a greater rate. Epinephrine and cortisol cause the breakdown of protein and lipids and the synthesis of glucose to help increase blood levels of nutrients. Growth hormone slows protein breakdown and favors lipid breakdown.

Testes and Ovaries

The testes of the male and the ovaries of the female secrete reproductive hormones, in addition to producing sperm cells or oocytes, respectively. The hormones produced by these organs play important roles in the development of sexual characteristics. Structural and functional differences between males and females, as well as the ability to reproduce, depend on the reproductive hormones (see table 10.2).

The main reproductive hormone in the male is **testosterone** (tes-TOSS-ter-ohn), which is secreted by the testes. It regulates the production of sperm cells by the testes and the development and maintenance of male reproductive organs and secondary sexual characteristics.

In the female, two main classes of reproductive hormones, secreted by the ovaries, affect sexual characteristics: (1) **estrogen** (ES-troh-jen) and (2) **progesterone** (proh-JESS-ter-ohn). These hormones, along with the anterior pituitary hormones, FSH and LH, control the female reproductive cycle, prepare the mammary glands for lactation, and maintain pregnancy. Estrogen and

progesterone are also responsible for the development of the female reproductive organs and female secondary sexual characteristics.

LH and FSH stimulate the secretion of hormones from the ovaries and testes. Releasing hormone from the hypothalamus controls the rate of LH and FSH secretion in males and females. LH and FSH, in turn, control the secretion of hormones from the ovaries and testes. Hormones secreted by the ovaries and testes also have a negative-feedback effect on the hypothalamus and anterior pituitary. The control of hormones that regulate reproductive functions is discussed in greater detail in chapter 19.

Thymus

The **thymus** lies in the upper part of the thoracic cavity (see figure 10.1 and table 10.2). It is important in the function of the immune system. The thymus secretes a hormone called **thymosin** (THIGH-moh-sin), which aids the development of white blood cells called T cells. T cells help protect the body against infection by foreign organisms. The thymus is most important early in life; if an infant is born without a thymus, the immune system does not develop normally, and the body is less capable of fighting infections (see chapter 14).

Pineal Gland

The **pineal** (PIN-ee-al; pinecone) **gland** is a small, pinecone-shaped structure located superior and posterior to the thalamus of the brain (see chapter 8). The pineal gland produces a hormone called **melatonin** (mel-ah-TONE-in). Melatonin is thought to inhibit the reproductive hypothalamic-releasing hormone, gonadotropin-releasing hormone. Inhibition of the hypothalamic-releasing hormone prevents secretion of the reproductive tropic hormones, LH and FSH from the anterior pituitary (see table 10.2). Thus, melatonin inhibits the reproductive system. Animal studies have demonstrated that the amount of available light controls the rate of melatonin secretion. In many animals, short day length causes an increase in melatonin secretion, whereas longer day length causes a decrease in melatonin secretion. Some people take melatonin supplements as a sleep aid. The function of the pineal gland in humans is not entirely clear, but tumors that destroy the pineal gland correlate with early sexual development, and tumors that result in pineal hormone secretion correlate with delayed development of the reproductive system. It is not known, however, if the pineal gland controls the onset of puberty.

Apply It 8

A tumor can destroy the pineal gland's ability to secrete melatonin. How would that affect the reproductive system of a young person?

10.7 OTHER HORMONES

Learning Outcomes *After reading this section, you should be able to*

A. Describe the functions of hormones secreted by the stomach and small intestine, the functions of prostaglandins, and the functions of erythropoietin.

Cells in the lining of the stomach and small intestine secrete hormones that stimulate the production of digestive juices from the stomach, pancreas, and liver. This secretion occurs when food is present in the digestive system, but not at other times. Hormones secreted from the small intestine also help regulate the rate at which food passes from the stomach into the small intestine (see chapter 16).

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SYSTEMS PATHOLOGY

Graves Disease (Hyperthyroidism)

Background Information

Over several months, Grace began to notice that she was sweating excessively and looking flushed. In addition, she often felt her heart pounding, was much more nervous than usual, and found it difficult to concentrate. Then Grace began to feel weak and lose weight, even though her appetite was greater than normal. Grace was diagnosed with Graves disease, a type of hyperthyroidism. Graves disease is caused by altered regulation of hormone secretion —specifically, the elevated secretion of thyroid hormones from the thyroid gland. In approximately 95% of Graves disease cases, the immune system produces an unusual antibody type, which binds to receptors on the cells of the thyroid follicle and stimulates them to secrete increased amounts of thyroid hormone. The secretion of the releasing hormone and thyroid-stimulating hormone is inhibited by elevated thyroid hormones. However, the antibody is produced in large amounts and is not inhibited by thyroid hormones. A very elevated rate of thyroid hormone secretion is therefore maintained. In addition, the size of the thyroid gland increases, and connective tissue components are deposited behind the eyes, causing them to bulge (figure 10.23). Enlargement of the thyroid gland is called a goiter.

Figure 10.23 Effects of Hyperthyroidism

(*a*) A goiter and (*b*) protruding eyes are symptoms of hyperthyroidism.

(a) ©Mike Goldwater/Alamy; (b) ©Ralph C. Eagle, Jr./Science Source

Grace was treated with radioactive iodine (^{131}I) atoms that were actively transported into thyroid cells, where they destroyed a substantial portion of the thyroid gland. Data indicate that this treatment has few side effects and is effective in treating most cases of Graves disease. Other options include (1) drugs that inhibit the synthesis and secretion of thyroid hormones and (2) surgery to remove part of the thyroid gland. Figure 10.24 illustrates the effects Graves disease may have on the body's organ systems.

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Figure 10.24 Interactions Among Organ Systems and Graves Disease

Graves disease affects many body systems, as this diagram illustrates.

Apply It 9

Explain why removal of part of the thyroid gland is an effective treatment for Graves disease.

TABLE 10.4 REPRESENTATIVE DISEASES AND DISORDERS: Endocrine System	
Condition	**Description**
Diabetes insipidus	Due to a lack of ADH from the posterior pituitary; results in excessive urination
Hashimoto thyroiditis	Autoimmune disease in which thyroid hormone secretion can be decreased; metabolic rate is decreased, weight gain is possible, and activity levels are depressed
Primary hyperparathyroidism	90% of cases due to adenoma of the parathyroid gland; causes blood PTH levels to increase above normal; elevated blood Ca^{2+} levels, weakened bones and possible muscular weakness
Addison disease	Low levels of aldosterone and cortisol from the adrenal cortex; low blood Na^{+} levels, low blood pressure, and excessive urination
Gestational diabetes	Develops in pregnant women due to actions of the placental hormone, human placental lactogen (HPL); in some women, HPL overly desensitizes the woman's insulin receptors; causes elevated blood glucose levels in the mother and, if left untreated, excessive fetal growth

EFFECTS OF AGING

THE ENDOCRINE SYSTEM

Age-related changes to the endocrine system include a gradual decrease in the secretion of some, but not all, endocrine glands. Some of the decreases in secretion may be due to the fact that older people commonly engage in less physical activity.

GH secretion decreases as people age. However, regular exercise offsets this decline. Older people who do not exercise have significantly lower GH levels than older people who exercise regularly. Decreasing GH levels may explain the gradual decrease in bone and muscle mass and the increase in adipose tissue seen in many elderly people. So far, administering GH to slow or prevent the consequences of aging has not been found to be effective, and unwanted side effects are possible.

A decrease in melatonin secretion may influence age-related changes in sleep patterns, as well as the decreased secretion of some hormones, such as GH and testosterone.

The secretion of thyroid hormones decreases slightly with age. Age-related damage to the thyroid gland by the immune system can occur. Approximately 10% of elderly women experience some reduction in thyroid hormone secretion; this tendency is less common in men.

The kidneys of the elderly secrete less renin, reducing the ability to respond to decreases in blood pressure.

Reproductive hormone secretion gradually declines in elderly men, and women experience menopause (see chapter 19).

Secretion of thymosin from the thymus decreases with age. Fewer functional lymphocytes are produced, and the immune system becomes less effective in protecting the body against infections and cancer.

Parathyroid hormone secretion increases to maintain blood calcium levels if dietary Ca^{2+} and vitamin D levels decrease, as they often do in the elderly. Consequently, a substantial decrease in bone matrix may occur.

In most people, the ability to regulate blood glucose does not decrease with age. However, there is an age-related tendency to develop type 2 diabetes mellitus for those who have a familial tendency, and it is correlated with age-related increases in body weight.

Prostaglandins are widely distributed in tissues of the body, where they function as intercellular signals. Unlike most hormones, they are usually not transported long distances in the blood but function mainly as autocrine or paracrine chemical signals (see table 10.1). Thus, their effects occur in the tissues where they are produced. Some prostaglandins cause relaxation of smooth muscle, such as dilation of blood vessels. Others cause contraction of smooth muscle, such as contraction of the uterus during the delivery of a baby. Because of their action on the uterus, prostaglandins have been used medically to initiate abortion. Prostaglandins also play a role in inflammation. They are released by damaged tissues and cause blood vessel dilation, localized swelling, and pain. Prostaglandins produced by platelets appear to be necessary for normal blood clotting. The ability of aspirin and related substances to reduce pain and inflammation, to help prevent the painful cramping of uterine smooth muscle, and to treat headache is a result of their inhibitory effect on prostaglandin synthesis.

The right atrium of the heart secretes atrial natriuretic hormone (ANH, also called ANP) in response to elevated blood pressure. ANH inhibits Na^{+} reabsorption in the kidneys. This causes more urine to be produced, reducing blood volume. Lowered blood volume lowers blood pressure (see chapter 18).

The kidneys secrete the hormone **erythropoietin** (eh-RITH-roh-POY-ee-tin) in response to reduced oxygen levels in the blood. Erythropoietin acts on bone marrow to increase the production of red blood cells (see chapter 11).

In pregnant women, the placenta is an important source of hormones that maintain pregnancy and stimulate milk production. These hormones are estrogen, progesterone, and **human chorionic gonadotropin** (GOH-nad-oh-TROH-pin),

which is similar in structure and function to LH. chapter 20 describes the function of these hormones in more detail.

SUMMARY

10.1 Principles of Chemical Communication

1. The four classes of chemical messengers are autocrine, paracrine, neurotransmitter, and endocrine.
2. Endocrine chemical messengers are called hormones.

10.2 Functions of the Endocrine System

The endocrine system has 10 major functions that contribute to homeostasis.

10.3 Hormones

Chemical Nature of Hormones

1. There are two chemical categories of hormones: lipid-soluble and water-soluble.
2. Lipid-soluble hormones include steroids, thyroid hormones, and some fatty acid derivatives.
3. Water-soluble hormones include proteins, peptides, and amino acid derivatives.
   - Water-soluble hormones circulate freely in the blood.
   - Proteases degrade protein and peptide hormones in the blood; the breakdown products are then excreted in the urine. However, some water-soluble hormones have chemical modifications, such as the addition of a carbohydrate group, which prolongs their life span.

10.4 Control of Hormone Secretion

Stimulation of Hormone Release

Three types of stimuli result in hormone secretion: humoral, neural, and hormonal.

1. Humoral stimulation is exhibited by hormones that are sensitive to circulating blood levels of certain molecules, such as glucose or calcium.

2. Neural stimuli cause hormone secretion in direct response to action potentials in neurons, as occurs during stress or exercise. Hormones from the hypothalamus that cause the release of other hormones are called releasing hormones.
3. Hormonal stimulation of other hormone secretion is common in the endocrine system. Hormones from the anterior pituitary that stimulate hormones from other endocrine glands are called tropic hormones.

Inhibition of Hormone Release

Although the stimulus of hormone secretion is important, inhibition is equally important.

1. Humoral substances can inhibit the secretion of hormones.
2. Neural stimuli can prevent hormone secretion.
3. Inhibiting hormones prevent hormone release.

Regulation of Hormone Levels in the Blood

Two processes regulate the overall blood levels of hormones: negative feedback and positive feedback.

1. Negative feedback prevents further hormone secretion once a set point is achieved.
2. Positive feedback is a self-promoting system whereby the stimulation of hormone secretion increases over time.

10.5 Hormone Receptors and Mechanisms of Action

Classes of Receptors

Each of the two groups of hormones has its own class of receptors.

1. Lipid-soluble hormones bind to nuclear receptors located inside the nucleus of the target cell. Some lipid-soluble hormones have rapid actions that are most likely mediated via a membrane-bound receptor.
2. Water-soluble hormones bind to membrane-bound receptors, which are integral membrane proteins.

Action of Nuclear Receptors

1. Nuclear receptors have portions that allow them to bind to the DNA in the nucleus once the hormone is bound.
   - The hormone-receptor complex activates genes, which in turn activate the DNA to produce mRNA.
   - The mRNA increases the synthesis of certain proteins that produce the target cell's response.

2. Nuclear receptors cannot respond immediately because it takes time to produce the mRNA and the protein.

Membrane-Bound Receptors and Signal Amplification

1. Membrane-bound receptors activate a cascade of events once the hormone binds.
2. Some membrane-bound receptors are associated with membrane proteins called G proteins. When a hormone binds to a membrane-bound receptor, G proteins are activated. The α subunit of the G protein can bind to ion channels and cause them to open or change the rate of synthesis of intracellular mediators, such as cAMP.
3. Second-messenger systems act rapidly because they act on already existing enzymes and produce an amplification effect.

10.6 Endocrine Glands and Their Hormones

1. The endocrine system consists of ductless glands.
2. Some glands of the endocrine system perform more than one function.

Pituitary and Hypothalamus

1. The pituitary is connected to the hypothalamus in the brain by the infundibulum. It is divided into anterior and posterior portions.
2. Secretions from the anterior pituitary are controlled by hormones that pass through the hypothalamic-pituitary portal system from the hypothalamus.
3. Hormones secreted from the posterior pituitary are controlled by action potentials carried by axons that pass from the hypothalamus to the posterior pituitary.
4. The hormones released from the anterior pituitary are growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, and melanocyte-stimulating hormone (MSH).
5. Hormones released from the posterior pituitary include antidiuretic hormone (ADH) and oxytocin.

Thyroid Gland

The thyroid gland secretes thyroid hormones, which control the metabolic rate of tissues, and calcitonin, which helps regulate blood Ca^{2+} levels.

Parathyroid Glands

The parathyroid glands secrete parathyroid hormone, which helps regulate blood Ca^{2+} levels. Active vitamin D also helps regulate blood Ca^{2+} levels.

Adrenal Glands

1. The adrenal medulla secretes primarily epinephrine and some norepinephrine. These hormones help prepare the body for physical activity.
2. The adrenal cortex secretes three classes of hormones.
   a. Glucocorticoids (cortisol) reduce inflammation and break down proteins and lipids, making them available as energy sources to other tissues.
   b. Mineralocorticoids (aldosterone) help regulate blood Na^+ and K^+ levels and water volume. Renin, secreted by the kidneys, helps regulate blood pressure by increasing angiotensin II and aldosterone production. These hormones cause blood vessels to constrict and enhance Na^+ and water retention by the kidney.
   c. Adrenal androgens increase female sexual drive but normally have little effect in males.

Pancreas, Insulin, and Diabetes

1. The pancreas secretes insulin in response to elevated levels of blood glucose and amino acids. Insulin increases the rate at which many tissues, including adipose tissue, the liver, and skeletal muscles, take up glucose and amino acids.
2. The pancreas secretes glucagon in response to reduced blood glucose and increases the rate at which the liver releases glucose into the blood.
3. The pancreas secretes somatostatin in response to food intake. Somatostatin inhibits insulin and glucagon secretion and gastric tract activity.

Testes and Ovaries

1. The testes secrete testosterone, and the ovaries secrete estrogen and progesterone. These hormones help control reproductive processes.
2. LH and FSH from the pituitary gland control hormone secretion from the ovaries and testes.

Thymus

The thymus secretes thymosin, which enhances the function of the immune system.

Pineal Gland

The pineal gland secretes melatonin, which may help regulate the onset of puberty by acting on the hypothalamus.

10.7 Other Hormones

1. Hormones secreted by cells in the stomach and intestine help regulate stomach, pancreatic, and liver secretions.
2. The prostaglandins are hormones that have a local effect, produce numerous effects on the body, and play a role in inflammation
3. ANH from the right atrium of the heart lowers blood pressure.
4. Erythropoietin from the kidney stimulates red blood cell production.
5. The placenta secretes human chorionic gonadotropin, estrogen, and progesterone, which are essential to the maintenance of pregnancy.

REMEMBERING AND UNDERSTANDING

1. What are the major functional differences between the endocrine system and the nervous system?
2. List the functions of the endocrine system.
3. List the major differences between intracellular and intercellular chemical signals.
4. List the intercellular chemical signals that are classified on the basis of the cells from which they are secreted and their target cells.
5. Explain the relationship between a hormone and its receptor.
6. Describe the mechanisms by which membrane-bound receptors produce responses in their target tissues.
7. Describe the mechanisms by which intracellular receptors produce responses in their target tissues.
8. Compare the means by which hormones that can and cannot cross the cell membrane produce a response.
9. Define endocrine gland and hormone.
10. What makes one tissue a target tissue for a hormone and another not a target tissue?
11. Into what chemical categories can hormones be classified?
12. Name three ways that hormone secretion is regulated.
13. Describe how secretions of the anterior and posterior pituitary hormones are controlled.

14. What are the functions of growth hormone? What happens when too little or too much growth hormone is secreted?
15. Describe the effect of gonadotropins on the ovary and testis.
16. What are the functions of the thyroid hormones, and how is their secretion controlled? What happens when too large or too small an amount of the thyroid hormones is secreted?
17. Explain how calcitonin, parathyroid hormone, and vitamin D are involved in maintaining blood Ca^{2+} levels. What happens when too little or too much parathyroid hormone is secreted?
18. List the hormones secreted from the adrenal gland, give their functions, and compare the means by which the secretion rate of each is controlled.
19. What are the major functions of insulin and glucagon? How is their secretion regulated? What is the effect if too little insulin is secreted or the target tissues are not responsive to insulin?
20. List the effects of testosterone, estrogen, and progesterone.
21. What hormones are produced by the thymus and by the pineal gland? Name the effects of these hormones.
22. List the effects of prostaglandins. How is aspirin able to reduce the severity of the inflammatory response?
23. List the hormones secreted by the placenta.
24. List the major age-related changes that affect the endocrine system.

CRITICAL THINKING

1. A hormone is known to bind to a membrane-bound receptor. If a drug that inhibits breakdown of cAMP is given, the response to the hormone is increased. If this is followed by giving a second drug that prevents GTP binding, the increased response to the hormone is reversed. Based on these observations, describe the mechanism by which the membrane-bound receptor is most likely to produce a response to the hormone.
2. Aldosterone and antidiuretic hormone play important roles in regulating blood volume and concentration of blood. The response to one of these hormones is evident within minutes, and the response to the other requires several hours. Explain the difference in response time for these two hormones.

3. Jordan figured that if a small amount of a vitamin was good, a lot should be better, so he began to take supplements that included a large amount of vitamin D. Explain the effect of vitamin D on his blood Ca^{2+} levels and on the secretion of hormones that regulate blood Ca^{2+} levels.
4. If a person's adrenal cortex degenerated and no longer secreted hormones, what would be the consequences?
5. Predict the effect of elevated aldosterone secretion from the adrenal cortex.
6. Explain how the blood levels of glucocorticoids, epinephrine, insulin, and glucagon change after a person has gone without food for 24 hours.
7. Stella wanted to go to medical school to become a physician. While attending college, she knew her grades had to be excellent. Stella worked very hard and worried constantly. By the end of each school year, she had a cold and suffered from stomach pains. Explain why she might be susceptible to these symptoms.

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

11

Blood

Blood is a fluid connective tissue composed of plasma, extracellular matrix, and formed elements, the cells of the tissue.

LEARN TO APPLY IT

Jessica didn't have time to be sick. She had so much to do, but she just hadn't felt well the past few weeks. At first she attributed her extreme tiredness to the stress of being a 40-year-old single mother of two teenagers while working full time and attending school part time. However, over the last few days she had started experiencing significant abdominal pain. Jessica decided it was time to consult her doctor. After she described her symptoms to her doctor, he ordered several tests. The results indicated a low red blood cell (RBC) count with microcytic RBCs, low hemoglobin and hematocrit levels, and evidence of hemoglobin in her feces.

After reading this chapter, explain Jessica's symptoms and test results.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 9 Cardiovascular System

11.1 FUNCTIONS OF BLOOD

Learning Outcomes *After reading this section, you should be able to*

A. State the functions of blood.

Blood has always fascinated humans, and throughout history they have speculated about its function. Some societies consider blood the "essence of life" because the uncontrolled loss of it can result in death. Many cultures around the world, both ancient and modern, believe blood has magical qualities. Blood has also been thought to define our character and emotions. For example, people of a noble bloodline are sometimes described as "blue bloods," whereas criminals are said to have "bad" blood. People commonly say that anger causes their blood to "boil," whereas fear makes it "curdle." The scientific study of blood reveals characteristics as fascinating as any of these fantasies. Blood performs many functions essential to life. Diagnostic tests that evaluate the blood composition can reveal much about our health. The heart pumps blood through blood vessels that extend throughout the body. Blood helps maintain homeostasis in several ways:

1. *Transport of gases, nutrients, and waste products.* Blood acts as a major transport medium in the body due to the many substances that move into and out of the blood. Substances can enter the blood in one area of the body, flow through blood vessels, and eventually leave the blood in a different area of the body. Oxygen enters the blood in the lungs and is carried to cells. Carbon dioxide, produced by cells, is carried in the blood to the lungs, from which it is expelled. The blood transports ingested nutrients, ions, and water from the digestive tract to cells, and the blood transports the waste products of the cells to the kidneys for elimination.
2. *Transport of processed molecules.* Many substances must be processed at multiple sites in the body. A substance may be produced in one organ or tissue, enter the blood and move to a new location where it is modified. For example, the precursor to vitamin D is produced in the skin (see chapter 5) and transported by the blood to the liver and then to the kidneys for processing into active vitamin D. Then the blood transports active vitamin D to the small intestine, where it promotes the uptake of calcium. Another example is lactate produced by skeletal muscles during anaerobic respiration (see chapter 7). The blood carries lactate to the liver, where it is converted into glucose.
3. *Transport of regulatory molecules.* The blood carries many of the hormones and enzymes that regulate body processes from one part of the body to another.
4. *Regulation of pH and osmosis.* Buffers (see chapter 2), which help keep the blood's pH within its normal limits of 7.35–7.45, are found in the blood. The osmotic composition of blood is also critical for maintaining normal fluid and ion balance.
5. *Maintenance of body temperature.* As blood flows through areas of the body that are metabolically active, the heat generated by metabolism warms the blood. Warm blood is transported from the interior of the body to the surface, where heat is released from the

blood. This is one of the mechanisms that helps regulate body temperature.

6. *Protection against foreign substances.* Certain cells and chemicals in the blood constitute an important part of the immune system, protecting against pathogens, such as certain microorganisms, as well as some toxins.
7. *Clot formation.* When blood vessels are damaged, blood clotting protects against excessive blood loss. When tissues are damaged, the blood clot that forms is also the first step in tissue repair and the restoration of normal function (see chapter 4).

11.2 COMPOSITION OF BLOOD

Learning Outcomes ***After reading this section, you should be able to***

A. List the components of blood.

Blood is a type of connective tissue that consists of a liquid matrix containing cells and cell fragments. The liquid matrix is the **plasma** (PLAZ-mah), and the cells and cell fragments are the **formed elements** (figure 11.1). The plasma accounts for slightly more than half (55%) of the total blood volume, and the formed elements account for slightly less than half (45%). The total blood volume is about 4–5 liters (L) in the average adult female and 5–6 L in the average adult male. Blood makes up about 8% of total body weight.

Figure 11.1 APR **Composition of Blood**

Approximate values for the components of blood in a normal adult.

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11.3 PLASMA

Learning Outcomes *After reading this section, you should be able to*

A. Name the components of plasma, and give their functions.

Plasma is a pale yellow fluid that consists of about 91% water, 7% proteins, and 2% other components, such as ions, nutrients, gases, waste products, and regulatory substances (figure 11.1 and table 11.1). Unlike the fibrous proteins found in other connective tissues, such as loose connective tissue, plasma contains dissolved proteins. Plasma proteins include (1) albumin, (2) globulins, and (3) fibrinogen. **Albumin** (al-BYOO-min) makes up 58% of the plasma proteins. Although the osmotic pressure (see chapter 3) of blood results primarily from Na^+ and Cl^-, albumin also makes an important contribution. The water balance between the blood and the tissues is determined by the movement of water into and out of the blood by osmosis, which is determined by solutes such as ions and plasma proteins. **Globulins** (GLOB-you-lins; globule) account for 38% of the plasma proteins. Some globulins, such as antibodies and complement, are part of the immune system (see chapter 14). Other globulins as well as albumin function as transport molecules. In this role, the plasma proteins bind to molecules, such as hormones (see chapter 10), and carry them in the blood throughout the body. In addition, some globulins are clotting factors, which are necessary for the formation of blood clots. **Fibrinogen** (fie-BRIN-oh-jen) is also a clotting factor that constitutes 4% of plasma proteins. Activation of clotting factors results in the conversion of fibrinogen to **fibrin** (FIE-brin), a threadlike protein that forms blood clots (see "Blood Clotting" in section 11.5). **Serum** (SEER-um) is plasma without the clotting factors.

TABLE 11.1 Composition of Plasma

Plasma Components	Functions and Examples
Water	Acts as a solvent and suspending medium for blood components
Proteins	Maintain osmotic pressure (albumin), destroy foreign substances (antibodies and complement), transport molecules (albumin and globulins), and form clots (fibrinogen)
Ions	Involved in osmotic pressure (Na^+ and Cl^-), membrane potentials (Na^+ and K+), and acid-base balance (hydrogen, hydroxide, and bicarbonate ions)
Nutrients	Source of energy and "building blocks" of more complex molecules (glucose, amino acids, triglycerides)
Gases	Involved in aerobic respiration (oxygen and carbon dioxide)

Plasma Components	Functions and Examples
Waste products	Breakdown products of protein metabolism (urea and ammonia salts) and red blood cells (bilirubin)
Regulatory substances	Catalyze chemical reactions (enzymes) and stimulate or inhibit many body functions (hormones)

Plasma volume and composition remain relatively constant. Normally, water intake through the digestive tract closely matches water loss through the kidneys, lungs, digestive tract, and skin. Oxygen and carbon dioxide are important "blood gases." Oxygen enters the blood in the lungs, and carbon dioxide enters the blood from tissues. Other suspended or dissolved substances in the blood come from the liver, kidneys, intestines, endocrine glands, and immune tissues, such as the lymph nodes and spleen. The concentration of these substances in the blood is also regulated and maintained within narrow limits.

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11.4 FORMED ELEMENTS

Learning Outcomes *After reading this section, you should be able to*

A. Describe the origin and production of the formed elements.
B. Describe the structure and function of red blood cells.
C. Describe the life history of a red blood cell.
D. Compare the structures and functions of the five types of white blood cells.
E. Describe the origin and structure of platelets.

As stated earlier, formed elements account for 45% of the total composition of blood. The formed elements include (1) red blood cells, (2) white blood cells, and (3) platelets. **Red blood cells (RBCs),** or *erythrocytes* (eh-RITH-roh-sites; *erythro-,* red + *kytos,* cell) are the most abundant of the formed elements. Red blood cells constitute nearly 95% of all the formed elements. The remaining 5% of the volume of the formed elements consists of **white blood cells (WBCs),** or *leukocytes* (LOO-koh-sites; *leuko-*, white), and cell fragments called **platelets** (PLAYT-lets), or *thrombocytes* (THROM-boh-sites; *thrombo-*, clot). Red blood cells are 700 times more numerous than white blood cells and 17

times more numerous than platelets. Table 11.2 illustrates the formed elements of the blood.

TABLE 11.2 Formed Elements of the Blood

Cell Type	Illustration	Description	Function
Red Blood Cell		Biconcave disk; no nucleus; contains hemoglobin, which colors the cell red; 6.5–8.5 µm in diameter	Transports O_2 and CO_2
White Blood Cells		Spherical cells with a nucleus	Five types of white blood cells, each with specific functions
Granulocytes			
Neutrophil		Nucleus with two to four lobes connected by thin filaments; cytoplasmic granules stain a light pink or reddish purple; 10–12 µm in diameter	Phagocytizes microorganisms and other substances
Basophil		Nucleus with two indistinct lobes; cytoplasmic granules stain blue-purple; 10–12 µm in diameter	Releases histamine, which promotes inflammation, and heparin, which prevents clot formation

Cell Type	Illustration	Description	Function
Eosinophil		Nucleus often bilobed; cytoplasmic granules stain orange-red or bright red; 11–14 µm in diameter	Participates in inflammatory response of allergic reactions and asthma; attacks certain worm parasites
Agranulocytes			
Lymphocyte		Round nucleus; cytoplasm forms a thin ring around the nucleus; 6–14 µm in diameter	Produces antibodies and other chemicals responsible for destroying microorganisms; contributes to allergic reactions, graft rejection, tumor control, and regulation of immune system
Monocyte		Nucleus round, kidney-shaped, or horseshoe-shaped; contains more cytoplasm than does lymphocyte; 12–20 µm in diameter	Phagocytic cell in the blood; leaves the blood and becomes a macrophage, which phagocytizes bacteria, dead cells, cell fragments, and other debris within tissues
Platelet		Cell fragment surrounded by a cell membrane and containing granules; 2–4 µm in diameter	Forms platelet plugs; releases chemicals necessary for blood clotting

Production of Formed Elements

Hematopoiesis (hee-MA-toh-poy-EE-sis; *hemato-,* blood + *poiesis,* making) is the process that produces formed elements. This process is continuous throughout our lives. In the fetus, hematopoiesis occurs in several tissues, including the liver, thymus, spleen, lymph nodes, and red bone marrow. After birth, hematopoiesis is confined primarily to red bone marrow, but some white blood cells are produced in lymphatic tissues (see chapter 14).

CLINICAL IMPACT

Stem Cells and Cancer Therapy

Many cancer therapies attack the types of rapidly dividing cells found in tumors. An undesirable side effect, however, can be the destruction of nontumor cells that divide rapidly, such as the stem cells and their derivatives in red bone marrow. After treatment for cancer, some patients are prescribed growth factors to stimulate the rapid regeneration of the red bone marrow. Although not a treatment for the cancer itself, the growth factors can speed recovery from the side effects of cancer therapy.

Some types of leukemia and genetic immune deficiency diseases can be treated with a bone marrow transplant containing blood stem cells. To avoid tissue rejection, families with a history of these disorders can freeze the umbilical cord blood of their newborn children. The cord blood contains many stem cells and can be used instead of a bone marrow transplant.

All the formed elements of blood are derived from a single population of cells called **hematopoietic stem cells,** or *hemocytoblasts*. These stem cells differentiate to give rise to two types of intermediate stem cells: (1) **myeloid stem cells** and (2) **lymphoid stem cells.** Most of the formed elements are derived from myeloid stem cells. Lymphoid stem cells give rise to lymphocytes, a type of white blood cell (figure 11.2). The development of each cell line is regulated by specific growth factors. That is, growth factors determine the types of formed elements

derived from the stem cells and how many formed elements are produced.

Figure 11.2 **Hematopoiesis**
Stem cells give rise to the cell lines that produce the formed elements.

Red Blood Cells

Normal red blood cells are disk-shaped, with edges that are thicker than the center of the cell (figure 11.3). The structure of a red blood cell is important to its function. Researchers have long proposed that the biconcave shape of a red blood cell increases the cell's surface area, thereby allowing gases to move into and out of the red blood cell more

rapidly as compared to a flat disc of the same size. Gases enter and leave red blood cells most often in small blood vessels called capillaries. As red blood cells move through capillaries, they change shape, so the relation of surface area to volume is not as obvious. But the fact that the cells change shape is of interest. Because of their biconcave shape, red blood cells can bend and fold around their thin centers, thereby decreasing in size and passing more easily through small vessels. In addition, research has shown that the biconcave disc shape of red blood cells may also improve blood flow in larger vessels.

Figure 11.3 APR **Red Blood Cells and White Blood Cells**

(*a*) Scanning electron micrograph of formed elements: red blood cells (*red doughnut shapes*) and white blood cells (*yellow*). (*b*) Shape and dimensions of a red blood cell.

(a) ©National Cancer Institute/Science Source

During their development, red blood cells lose their nuclei and most of their organelles. Consequently, they are unable to divide. Red blood cells live for about 120 days in males and 110 days in females. One-third of a red blood cell's volume is the pigmented protein **hemoglobin** (HEE-moh-GLOH-bin), which is responsible for the cell's red color.

Function

The primary functions of red blood cells are to transport O_2 from the lungs to the various tissues of the body and to help transport CO_2 from the tissues to the lungs. Oxygen transport is accomplished when O_2 enters red blood cells and binds to hemoglobin. Each hemoglobin molecule consists of four protein chains and four heme groups (figure

11.4). Each protein chain, called a **globin** (GLOH-bin), is bound to one **heme** (HEEM), a red-pigmented molecule. Each heme contains one iron atom, which is necessary for the normal function of hemoglobin. The iron atom in a heme molecule can reversibly bind to an oxygen molecule. A single red blood cell contains many molecules of hemoglobin, allowing for transport of sufficient O_2 to the cells of the body. Hemoglobin picks up O_2 in the lungs and releases O_2 in other tissues (see chapter 15). Hemoglobin that is bound to O_2 is bright red, whereas hemoglobin without bound O_2 is a darker red. 98.5% of the O_2 transported in blood is bound to hemoglobin molecules within red blood cells. The remaining 1.5% of O_2 is dissolved in plasma.

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Figure 11.4 APR **Hemoglobin**

(*a*) Hemoglobin consists of four subunits, each with a globin and a heme. There are two alpha (α) globins and two beta (β) globins. A heme is associated with each globin. (*b*) Each heme contains one iron atom.

Because iron is necessary for O_2 transport, it is not surprising that two-thirds of the body's iron is found in hemoglobin. Small amounts of iron are required in the diet to replace the small amounts lost in the urine and feces, but otherwise the existing iron is recycled, as described later in this section. Females need more dietary iron than males do because females lose iron as a result of menstruation.

Although O_2 is the primary molecule that binds to hemoglobin, other molecules can also bind to hemoglobin. Carbon monoxide (CO), a gas produced by the incomplete combustion of hydrocarbons, such as

gasoline, is one example. It binds to the iron in hemoglobin about 210 times more readily than does O_2 and does not tend to unbind. As a result, the hemoglobin bound to carbon monoxide no longer transports O_2. Nausea, headache, unconsciousness, and death are possible consequences of prolonged exposure to carbon monoxide.

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Carbon dioxide is produced in tissues and transported in the blood to the lungs, where it is removed from the blood (see chapter 15). Carbon dioxide transport involves bicarbonate ions, hemoglobin, and plasma. Approximately 70% of the CO_2 in blood is transported in the form of bicarbonate ions. The enzyme **carbonic anhydrase** (kar-BON-ik an-HIGH-drase), found primarily inside red blood cells, catalyzes a reaction that converts carbon dioxide (CO_2) and water (H_2O) into a hydrogen ion (H^+) and a bicarbonate ion (HCO_3^-):

$$CO_2 + H_2O \rightleftarrows H^+ + HCO_3^-$$

The remaining 30% of CO_2 is transported two ways, (1) bound to proteins and (2) dissolved in the plasma. About 23% of the CO_2 in blood is transported bound to hemoglobin or other blood proteins. Carbon dioxide does not bind to the same area of hemoglobin molecules as O_2. Instead, CO_2 binds reversibly to the globin part of the hemoglobin. The remaining 7% of CO_2 is transported dissolved in plasma.

Life History of Red Blood Cells

Under normal conditions, about 2.5 million red blood cells are destroyed every second. Fortunately, new red blood cells are produced just as rapidly. Stem cells form **proerythroblasts** (PROH-eh-RITH-roh-blasts; *pro-,* before + *erythro-,* red + *blastos,* germ), which give rise to the red blood cell line (figure 11.5). Red blood cell production involves a series of cell divisions. After each cell division, the new cells change and become more like mature red blood cells. In the later divisions, the newly formed cells manufacture large amounts of hemoglobin. After the final cell division, the cells lose their nuclei and become completely mature red blood cells.

Myeloid stem cell
Proerythroblast
Early erythroblast
Intermediate erythroblast
Late erythroblast
Nucleus extruded
Reticulocyte
Red blood cell

Figure 11.5 **Red Blood Cell Production.**

Red blood cells are derived from myeloid stem cells. Under certain conditions, myeloid stem cells give rise to proerythroblasts, the first in a series of cells of the red blood cell lineage. With each step in the series, the new cells appear more like a red blood cell. In the final steps, the cell sheds its nucleus and eventually becomes a mature red blood cell.

Red blood cell production depends on the presence of several vitamins as well as sufficient iron. The process of cell division that produces new red blood cells requires the B vitamins folate and B_{12}, which are necessary for the synthesis of DNA (see chapter 3). Iron is required for the production of hemoglobin. Consequently, a lack of folate, vitamin B_{12}, or iron can interfere with normal red blood cell production.

Red blood cell production is stimulated by low blood O_2 levels. Typical causes of low blood O_2 are decreased numbers of red blood cells, decreased or defective hemoglobin, diseases of the lungs, inability of the cardiovascular system to deliver blood to tissues, as well as moving to a higher altitude and increased tissue demand for O_2, as occurs during endurance exercises.

Red blood cell production is regulated to ensure that homeostatic levels of these cells are present in the blood. Low blood O_2 levels stimulate red blood cell production by increasing the formation and release of the glycoprotein **erythropoietin** (eh-RITH-roh-POY-ee-tin, **EPO**), primarily by the kidneys (figure 11.6). Erythropoietin stimulates red bone marrow to produce more red blood cells. Thus, when O_2 levels in the blood decrease, the production of erythropoietin increases, which increases red blood cell production. The greater number of red blood cells increases the blood's ability to transport O_2. This negative-feedback mechanism increases the blood's capacity to transport O_2 and maintains homeostasis. Conversely, if blood O_2 levels rise, less erythropoietin is released, and red blood cell production decreases.

Figure 11.6 APR **Regulation of Red Blood Cell Production**

In response to decreased blood oxygen, the kidneys release erythropoietin into the general circulation. The increased erythropoietin stimulates red blood cell production in the red bone marrow. This process increases blood oxygen levels.

Analyze

Apply It 1

Cigarette smoke produces carbon monoxide. If a nonsmoker smoked a pack of cigarettes a day for a few weeks, what would happen to the number of red blood cells in the person's blood? Explain.

When red blood cells become old, abnormal, or damaged, they are removed from the blood by macrophages located in the spleen and liver. After phagocytosis, the hemoglobin is broken down and its components are recycled or excreted from the body. Figure 11.7 illustrates how the body processes the hemoglobin released from the engulfed red blood cells.

❶ *Macrophage breaks down hemoglobin*. The breakdown of hemoglobin begins in the cytoplasm of the macrophages. The globin chains and heme groups are separated.

❷ *Globin chain processing*. The globin part of the hemoglobin molecule is broken down into amino acids that are reused to produce other proteins.

❸ *Heme group breakdown*. The iron is released from each heme group.

❹ *Iron recycling*. The released iron atoms are then transported in the blood to the red bone marrow to be used to produce new hemoglobin. Thus, the iron is recycled.

❺ *Bilirubin production*. The heme molecules (minus iron) are converted to **bilirubin** (bill-ee-RU-bin), a yellow pigment molecule.

❻ *Liver excretion of bilirubin*. Bilirubin is normally removed from the blood by the liver and released into the small intestine as part of the bile (see chapter 16). If the liver is not functioning normally, or if the flow of bile from the liver to the small intestine is hindered, bilirubin builds up in the blood. As a consequence, bilirubin can be deposited into other tissues, resulting in a condition called **jaundice** (JAWN-dis; *jaune,* yellow), a yellowish color to the skin.

❼ *Bilirubin excretion as part of feces*. Under normal conditions, after bilirubin enters the intestine, it is converted by bacteria into other pigments. Some of these pigments give feces their brown color, whereas others may be absorbed from the intestine into the blood.

❽ *Bilirubin excretion as part of urine*. The pigments that are absorbed are modified by the kidneys and excreted in the urine, contributing to the characteristic yellow color of urine.

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PROCESS Figure

PROCESS Figure 11.7 APR **Hemoglobin Breakdown**

Macrophages break down hemoglobin, and the breakdown products are used or excreted.

Apply **In some forms of anemia, the red blood cells are fewer in number and smaller. Individuals with these forms of anemia produce feces that are light or white in color. Explain why this is expected.**

White Blood Cells

White blood cells are spherical cells that lack hemoglobin. When the components of blood are separated from one another, white blood cells as well as platelets make up the **buffy coat,** a thin, white layer of cells between plasma and red blood cells (see figure 11.1). White blood cells are larger than red blood cells, and each has a nucleus (table 11.2). Although white blood cells are components of the blood, the blood serves primarily as a means of transporting these cells to other body tissues. White blood cells can leave the blood and travel by **ameboid** (ah-MEE-boid; like an ameba) **movement** through the tissues. In this process, the cell projects a cytoplasmic extension that attaches to an object. Then the rest of the cell's cytoplasm flows into the extension. Two functions of white blood cells are (1) to protect the body against invading microorganisms and other pathogens and (2) to remove dead cells and debris from the tissues by phagocytosis.

Though all normal red blood cells are similar in shape and function, this is not the case with white blood cells. Instead, there are multiple types of white blood cells. Each white blood cell type is named according to its appearance in stained preparations. Those containing large cytoplasmic granules are *granulocytes* (GRAN-you-loh-sites; *granulo-,* granular), and those with very small granules that cannot be seen easily with the light microscope are **agranulocytes** (ay-GRAN-you-loh-sites; *a-,* without).

There are three kinds of granulocytes: (1) neutrophils, (2) basophils, and (3) eosinophils. **Neutrophils** (NEW-troh-fills; *neutro-,* neutral + *philos,* loving), the most common type of white blood cells, have small cytoplasmic granules that stain with both acidic and basic dyes (figure 11.8 and figure 11.9*a*). Their nuclei are commonly lobed, with the number of lobes varying from two to four. Neutrophils usually remain in the blood for a short time (10–12 hours), move into other tissues, and phagocytize microorganisms and other foreign substances. Dead neutrophils, cell debris, and fluid can accumulate as **pus** at sites of infections.

Figure 11.8 APR **Standard Blood Smear**

A thin film of blood is spread on a microscope slide and stained. The white blood cells have pink cytoplasm and purple nuclei. The red blood cells do not have nuclei. The center of a red blood cell appears whitish because light shines more readily through the thin center of the disk than through the thicker edges. The platelets are purple cell fragments.

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Figure 11.9 APR **Types of White Blood Cells**

(*a*) Neutrophil, (*b*) basophil, (*c*) eosinophil, (*d*) lymphocyte, (*e*) monocyte/macrophage. (a–e)

©Victor Eroschenko

Basophils (BAY-so-fills; *baso-,* base), the least common of all white blood cells, contain large cytoplasmic granules that stain blue or purple with basic dyes (figure 11.9*b*, table 11.2). Basophils release histamine and other chemicals that promote inflammation (see chapters 4 and 14). They also release heparin, which prevents the formation of clots.

Eosinophils (ee-oh-SIN-oh-fills) contain cytoplasmic granules that stain bright red with eosin, an acidic stain. They often have a two-lobed nucleus (figure 11.9*c*, table 11.2). Eosinophils are involved in inflammatory responses associated with allergies and asthma. In

addition, chemicals from eosinophils are involved in destroying certain worm parasites.

There are two kinds of agranulocytes: (1) lymphocytes and (2) monocytes. **Lymphocytes** (LIM-foh-sites; *lympho-,* lymph) are the smallest of the white blood cells (figure 11.9*d*, table 11.2). The lymphocytic cytoplasm consists of only a thin, sometimes imperceptible ring around the nucleus. There are various types of lymphocytes, and each type plays an important role in the body's immune response. Lymphocyte activities include the production of antibodies and other chemicals. The antibodies and other chemicals destroy microorganisms, contribute to allergic reactions, reject grafts, control tumors, and regulate the immune system. Chapter 14 considers lymphocytes and their roles in immunity in more detail.

CLINICAL IMPACT

Clinical Importance of Activating Platelets

Platelet activation results in platelet plug formation and the production of chemicals, such as phospholipids, that are important for blood clotting. Thus, inhibition of platelet activation reduces the formation of blood clots.

Thromboxanes, which activate platelets, are derived from certain prostaglandins. Aspirin inhibits prostaglandin synthesis and, therefore, thromboxane synthesis, which results in reduced platelet activation. If an expectant mother ingests aspirin near the end of pregnancy, thromboxane synthesis is inhibited. As a result, the mother experiences excessive bleeding after delivery, and the baby can exhibit numerous localized hemorrhages over the surface of its body, both due to decreased platelet function. If the quantity of ingested aspirin is large, the infant, the mother, or both may die as a result of bleeding.

Platelet plugs and blood clots can block blood vessels, producing heart attacks and strokes. Suspected heart attack victims are routinely given aspirin en route to the emergency room as part of their treatment. The United States Preventive Services Task Force (USPSTF) and the American Heart Association recommend low-dose aspirin therapy (75–160 mg/day) for all men and women at high risk for cardiovascular disease. Determining high risk involves analyzing many factors and should be done in consultation with a physician. The decreased risk of cardiovascular disease from aspirin therapy must be weighed against the increased

risk of hemorrhagic stroke and gastrointestinal bleeding. Risk factors include age (men over 40 and postmenopausal women), high cholesterol, high blood pressure, a history of smoking, diabetes, a family history of cardiovascular disease, and a previous clotting event, such as a heart attack, a transient ischemic attack, or an occlusive stroke.

Plavix (clopidogrel bisulfate) is a drug that reduces the activation of platelets by blocking the ADP receptors on the surface of platelets. It is administered to prevent clotting and, along with other anticlotting drugs, to treat heart attacks.

Monocytes (MON-oh-sites) are the largest of the white blood cells (figure 11.9*e*, table 11.2). After monocytes leave the blood and enter tissues, they enlarge and become **macrophages** (MAK-roh-fayjez; *macro-,* large + *phagō,* to eat), which phagocytize bacteria, dead cells, cell fragments, and any other debris within the tissues. In addition, macrophages can break down phagocytized foreign substances and present the processed substances to lymphocytes, causing activation of the lymphocytes (see chapter 14).

Apply It 2

White blood cells demonstrate the characteristic of positive chemotaxis, meaning they move toward certain signals. Considering their function, why is this characteristic important?

Platelets

Platelets are minute fragments of cells, each consisting of a small amount of cytoplasm surrounded by a cell membrane (see figure 11.8). They are produced in the red bone marrow from large cells called megakaryocytes (MEG-ah-KAIR-ee-oh-sites; *mega-,* large + *karyon,* nucleus) (see figure 11.2). Small fragments break off from the megakaryocytes and enter the blood as platelets. Platelets play an important role in preventing blood loss.

11.5 PREVENTING BLOOD LOSS

Learning Outcomes ***After reading this section, you should be able to***

A. Explain the formation and function of platelet plugs.

B. Distinguish between a platelet plug and a blood clot.
C. Describe the process of blood clotting.
D. Describe the regulation of clot formation.
E. Explain how clots are removed.

When a blood vessel is damaged, blood can leak into other tissues and interfere with normal tissue function, or blood can be lost from the body. The body can tolerate a small amount of blood loss and can produce new blood to replace it. But a large amount of blood loss can lead to death. Fortunately, when a blood vessel is damaged, loss of blood is minimized by three processes: (1) vascular spasm, (2) platelet plug formation, and (3) blood clotting.

Vascular Spasm

Vascular spasm is an immediate but temporary constriction of a blood vessel that results when smooth muscle within the wall of the blood vessel contracts. This constriction can close small blood vessels completely and stop the flow of blood through them. Vascular spasm is stimulated by chemicals released by cells of the damaged blood vessel wall and by platelets. For example, platelets release **thromboxanes** (THROM-bok-zanes), which are derived from certain prostaglandins. Also, endothelial (epithelial) cells lining blood vessels release the peptide **endothelin** (en-doh-THEE-lin). Both of these substances stimulate vascular spasm.

Platelet Plug Formation

A **platelet plug** is an accumulation of platelets that can seal up a small break in a blood vessel. Platelet plug formation is very important in maintaining the integrity of the blood vessels of the cardiovascular system because small tears occur in the smaller vessels and capillaries many times each day. People who lack the normal number of platelets tend to develop numerous small hemorrhages in their skin and internal organs.

The formation of a platelet plug can be described as a series of steps, but in actuality many of these steps occur at the same time Figure 11.10 illustrates the process of platelet plug formation.

❶ *Platelet adhesion*. Platelets stick to the collagen exposed by blood vessel damage. Most platelet adhesion is mediated through **von**

Willebrand factor, a protein produced and secreted by blood vessel endothelial cells. Von Willebrand factor forms a bridge between collagen and platelets by binding to platelet surface receptors and collagen. After platelets adhere to collagen, they become activated, change shape, and release chemicals.

❷ *Platelet release reaction*. Platelets release chemicals, such as ADP and thromboxane, which bind to their respective receptors on the surfaces of other platelets, activating the platelets. These activated platelets also release ADP and thromboxane, which activates more platelets. Thus, a cascade of chemical release activates many platelets. This is an example of positive feedback. As platelets become activated, they express surface receptors called **fibrinogen receptors,** which can bind to fibrinogen, a plasma protein.

❸ *Platelet aggregation*. Fibrinogen forms bridges between the fibrinogen receptors of numerous platelets, resulting in a platelet plug.

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PROCESS Figure

PROCESS Figure 11.10 **Platelet Plug Formation**

During platelet plug formation, platelets adhere to the surface of the damaged vessel and to other platelets to reduce blood loss.

Among other effects, aspirin inhibits thromboxane activity. How will this affect platelet plug formation?

Blood Clotting

Blood vessel constriction and platelet plugs alone are not sufficient to close large tears or cuts in blood vessels. When a blood vessel is severely damaged, **blood clotting,** or *coagulation* (koh-ag-you-LAY-shun), results in the formation of a clot. A **clot** is a network of threadlike protein fibers, called **fibrin,** that traps blood cells, platelets, and fluid.

The formation of a blood clot depends on a number of proteins found within plasma, called **clotting factors.** Though normally present in the plasma, the clotting factors are inactive and do not cause clotting. Following injury, however, the clotting factors are activated. Clot formation is a complex process involving many chemical reactions, but it can be summarized in three stages. Figure 11.11 illustrates the stages of clot formation.

1. *Prothrombinase production*. The chemical reactions necessary for blood clotting can be started in two ways: (a) Inactive clotting factors come in contact with exposed connective tissue, resulting in their activation, or (b) chemicals, such as **thromboplastin,** are released from injured tissues, causing activation of clotting factors. After the initial clotting factors are activated, they in turn activate other clotting factors. A series of reactions results in which each clotting factor activates the next until the clotting factor **prothrombinase** (PROH-throm-bi-nays), or *prothrombin activator*, is formed.
2. *Thrombin production*. Prothrombinase converts an inactive clotting factor called **prothrombin** (proh-THROM-bin) to its active form, **thrombin** (THROM-bin).
3. Fibrin production. Thrombin converts the plasma protein **fibrinogen** to fibrin.

PROCESS Figure

PROCESS Figure 11.11 **Blood Clot Formation**

Blood clot formation has three stages. During the formation of a clot, a complex series of chemical reactions ultimately results in the conversion of fibrinogen to fibrin.

Hemophilia is a genetic disease that affects clotting factor production. At which step in figure 11.11 would clot formation be most affected by hemophilia? Explain your answer.

At each step of the clotting process, each clotting factor activates many additional clotting factors, resulting in the formation of a blood clot.

Most clotting factors are manufactured in the liver, and many of them require vitamin K for their synthesis. In addition, many of the chemical

reactions of clot formation require Ca^{2+} and the chemicals released from platelets. Many factors, therefore, can affect the clotting process, including low levels of vitamin K, low levels of Ca^{2+}, low numbers of platelets, or liver dysfunction that reduces clotting factor production.

Humans rely on two sources of vitamin K. About half comes from the diet, and the other half comes from bacteria within the large intestine. Antibiotics taken to fight bacterial infections sometimes kill these intestinal bacteria, reducing vitamin K levels and causing bleeding problems. Vitamin K supplements may be necessary for patients on prolonged antibiotic therapy. Newborns lack these intestinal bacteria and thus routinely receive a vitamin K injection at birth. Infants can also obtain vitamin K from food, such as milk. Because cow's milk contains more vitamin K than does human milk, breast-fed infants are more susceptible to bleeding than are bottle-fed infants. However, maternal supplementation with vitamin K, such as with oral vitamins, adequately elevates breast-fed infant vitamin K levels and decreases the risk of bleeding.

Control of Clot Formation

Without control, clotting would spread from the point of its initiation throughout the blood vessels. Fortunately, the blood contains several **anticoagulants** (AN-tee-koh-AG-you-lants), which prevent clotting factors from forming clots under normal conditions. For example, **antithrombin** (an-tee-THROM-bin) and **heparin** (HEP-ah-rin) inactivate thrombin. Without thrombin, fibrinogen is not converted to fibrin, and no clot forms. At an injury site, however, the activation of clotting factors is very rapid. Enough clotting factors are activated that the anticoagulants can no longer prevent a clot from forming. Away from the injury site, there are enough anticoagulants to prevent clot formation from spreading.

In some instances, unwanted clots may form. When platelets encounter damaged or diseased areas of blood vessels or heart walls, an attached clot, called a **thrombus** (THROM-bus), can form. A thrombus that breaks loose and begins to float through the circulation is called an **embolus** (EM-boh-lus). Both thrombi and emboli can cause death if they block vessels that supply blood to certain organs, such as the heart, brain, or lungs. Abnormal coagulation can be prevented or hindered by administering an anticoagulant such as heparin, which acts rapidly.

Warfarin (WAR-fah-rin), brand name Coumadin (KOO-mah-din), acts more slowly than heparin. Warfarin prevents clot formation by suppressing the liver's production of vitamin K–dependent clotting factors.

Clot Retraction and Fibrinolysis

After a clot has formed, it begins to condense into a more compact structure through a process known as **clot retraction.** Platelets contain the contractile proteins actin and myosin, which operate in a fashion similar to that of the actin and myosin in muscle (see chapter 7). Platelets form small extensions that attach to fibrin through surface receptors. Contraction of the extensions pulls on the fibrin and leads to clot retraction. During clot retraction, serum, which is plasma without the clotting factors, is squeezed out of the clot.

Retraction of the clot pulls the edges of the damaged blood vessel together, helping stop the flow of blood, reducing the probability of infection, and enhancing healing. The vessel is repaired as fibroblasts move into the damaged area and new connective tissue forms. In addition, epithelial cells around the wound divide and fill in the torn area (see chapter 4).

Later, as the damaged tissue is repaired, clots are dissolved by a process called **fibrinolysis** (fih-bri-NOL-uh-sis). An inactive plasma protein called **plasminogen** (plaz-MIN-oh-jen) is converted to its active form, **plasmin** (PLAZ-min). Thrombin, other clotting factors activated during clot formation, and **tissue plasminogen activator (t-PA)** released from surrounding tissues can stimulate the conversion of plasminogen to plasmin. Over a few days, plasmin slowly breaks down the fibrin.

A heart attack can result when a clot blocks blood vessels that supply the heart. One treatment for a heart attack is to inject certain chemicals into the blood that activate plasmin. Unlike aspirin and anticoagulant therapies, which are used to prevent heart attacks, plasmin activators quickly dissolve the clot and restore blood flow to cardiac muscle, thus reducing damage to tissues. **Streptokinase** (strep-toh-KIN-ase), a bacterial enzyme, and t-PA, produced through genetic engineering, have been used successfully to dissolve clots.

11.6 BLOOD GROUPING

Learning Outcomes *After reading this section, you should be able to*

A. Define blood group.
B. Explain the basis of the ABO blood group.
C. Describe the Rh blood group.
D. Explain the basis of ABO and Rh incompatibilities.

If large quantities of blood are lost during surgery or due to injury, a patient can go into shock and die unless red blood cells are replaced to restore the blood's oxygen-carrying capacity. In this event, either a transfusion or an infusion is called for. A **transfusion** is the transfer of blood or blood components from one individual to another. An **infusion** is the introduction of a fluid other than blood, such as a saline or glucose solution, into the blood. In many cases, the return of blood volume to normal levels is all that is necessary to prevent shock. Eventually, the body produces enough red blood cells to replace those that were lost.

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Early attempts to transfuse blood were often unsuccessful because they resulted in **transfusion reactions,** characterized by clumping or rupture of blood cells and clotting within blood vessels. We now know that transfusion reactions are caused by interactions between antigens and antibodies (see chapter 14). In brief, the surfaces of red blood cells have molecules called **antigens** (AN-tih-jens), and the plasma includes proteins called **antibodies** (AN-tee-bod-ees; *anti-,* against). Antibodies bind to antigens; however, antibodies are very specific, meaning that each antibody can bind only to a certain antigen. When the antibodies in the plasma bind to the antigens on the surface of the red blood cells, they form molecular bridges that connect the red blood cells together. As a result, **agglutination** (ah-glue-tih-NAY-shun; *ad,* to + *gluten,* glue), or clumping of the cells, occurs. The combination of the antibodies with the antigens can also initiate reactions that cause **hemolysis** (hee-MOL-ih-sis; *hemo-,* blood + *lysis,* destruction), or rupture of the red blood cells. The debris formed from the ruptured red blood cells can cause severe tissue damage, particularly in the kidneys. Hemoglobin released from lysed red blood cells can also damage kidney tissue, reducing its blood-filtering ability. If the damage is extensive, the lack of kidney function could result in death.

The antigens on the surface of red blood cells have been categorized into **blood groups.** Although many blood groups are recognized, the ABO and Rh blood groups are the most important when discussing transfusion reactions.

ABO Blood Group

The **ABO blood group** system is used to categorize human blood. In this blood group system, there are two types of antigens that may appear on the surface of the red blood cells, (1) type A antigen and (2) type B antigen. Type A blood has type A antigens, type B blood has type B antigens, and type AB blood has both types of antigens. Type O blood has neither A nor B antigens (figure 11.12). Note that the "O" represents the absence of A and B antigens and does not represent a different antigen. The types of antigens found on the surface of the red blood cells are genetically determined.

Figure 11.12 ABO Blood Groups

There are four ABO blood types: type A, type B, type AB, and type O. Based on the blood type, one can predict whether or not anti-A and/or anti-B antibodies are present in the plasma.

Antibodies are present in the plasma of blood (see section 11.3, Plasma). Antibodies are part of the body's defense system and interact with specific antigens. A person produces antibodies for "foreign" antigens, meaning antigens that she does not possess. Transfusion reactions can therefore occur if a person receives blood that does not match her blood type. This is because plasma from type A blood contains anti-B antibodies, which act against type B antigens. Similarly, plasma from type B blood contains anti-A antibodies, which act against type A antigens. Type AB blood plasma has neither type of antibody, and type O blood plasma has both anti-A and anti-B antibodies. Review figure 11.12 for a visual representation of the combinations of antigens and antibodies for the ABO blood types.

The ABO blood types do not exist in equal numbers. In white individuals in the United States, the distribution is type O, 47%; type A, 41%; type B, 9%; and type AB, 3%. Among black individuals, the distribution is type O, 46%; type A, 27%; type B, 20%; and type AB, 7%.

Normally, antibodies do not develop against an antigen unless the body is exposed to that antigen; however, the anti-A and/or anti-B antibodies are present in the blood even without exposure to antigens on foreign red blood cells. One possible explanation for the production of anti-A and/or anti-B antibodies is that type A or B antigens on bacteria or food in the digestive tract stimulate the formation of antibodies against antigens that are different from the body's own antigens. In support of this explanation, anti-A and anti-B antibodies are not found in the blood until about 2 months after birth. It is possible that an infant with type A blood would produce anti-B antibodies against the B antigens on bacteria or food. Meanwhile, an infant with A antigens would not produce antibodies against the A antigens on bacteria or food because mechanisms exist in the body to prevent the production of antibodies that would react with the body's own antigens (see chapter 14).

When a blood transfusion is performed, the **donor** is the person who gives blood, and the **recipient** is the person who receives it. Usually, a recipient can successfully receive blood from a donor as long as they both have the same blood type. For example, a person with type A blood can receive blood from a person with type A blood. No ABO transfusion reaction occurs because the recipient has no anti-A antibodies against the type A antigen. On the other hand, if type A blood were donated to a person with type B blood, a transfusion reaction would occur because the

person with type B blood has anti-A antibodies against the type A antigen, causing agglutination (figure 11.13).

Figure 11.13 Agglutination Reaction

If a patient is transfused with the wrong blood type, an agglutination reaction occurs in which antibodies in the plasma interact with antigens on red blood cells of the donated blood.

Historically, people with type O blood have been called universal donors because they can usually give blood to the other ABO blood types without causing an ABO transfusion reaction. Their red blood cells have neither the type A nor the type B antigens and therefore do not react with the recipient's anti-A or anti-B antibodies. For example, if a person with type A blood receives type O blood, the type O red blood cells do not react with the anti-B antibodies in the recipient's blood.

However, the term *universal* donor is misleading. Transfusion of type O blood can still produce a transfusion reaction in one of two ways: First, mismatching blood groups other than the ABO blood group can cause a transfusion reaction. To reduce the likelihood of a transfusion reaction, all the blood groups must be correctly matched (see "Type and Crossmatch" in section 11.7). Second, antibodies in the donor's blood can react with antigens on the recipient's red blood cells. For example, type O blood has anti-A and anti-B antibodies. If type O blood is transfused into a person with type A blood, the anti-A antibodies (in the type O donor

blood) react against the A antigens (on the red blood cells in the type A recipient blood). Usually, such reactions are not serious because the antibodies in the donor's blood are diluted in the large volume of the recipient's blood. Even though such transfusion reactions seldom occur, type O blood is given to a person with another blood type only in life-or-death situations.

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Apply It 3

Historically, people with type AB blood were called universal recipients. What is the rationale for this term? Explain why the term is misleading.

Rh Blood Group

Another important blood group is the **Rh blood group,** so named because it was first studied in the rhesus monkey. People are Rh-positive if they have certain Rh antigens on the surface of their red blood cells, and they are Rh-negative if they do not have these Rh antigens. About 85% of white individuals and 95% of black individuals are Rh-positive. The ABO blood type and the Rh blood type are usually designated together. For example, a person designated as type A in the ABO blood group and Rh-positive is said to be A-positive. The rarest combination in the United States is AB-negative, which occurs in less than 1% of the population.

Apply It 4

Using a method similar to that in figure 11.12, illustrate the antigens present on a red blood cell from an individual who is B-positive.

As stated earlier, the antibodies for the A and B antigens are found in the plasma of blood even when a person has not been exposed to blood of a different blood type. This is not the case with the Rh antigens. Antibodies against the Rh antigens do not develop unless an Rh-negative person is exposed to Rh-positive red blood cells. This can occur through a

transfusion or by the transfer of blood across the placenta to a mother from her fetus. When an Rh-negative person receives a transfusion of Rh-positive blood, the recipient becomes sensitized to the Rh antigens and produces anti-Rh antibodies. If the Rh-negative person is unfortunate enough to receive a second transfusion of Rh-positive blood after becoming sensitized, a transfusion reaction results.

Rh incompatibility can pose a major problem in a pregnancy when the mother is Rh-negative and the fetus is Rh-positive. Any anti-Rh antibodies produced by the mother may cross the placenta and destroy fetal red blood cells. This disorder is called **hemolytic** (hee-moh-LIT-ik) **disease of the newborn (HDN),** or *erythroblastosis fetalis* (eh-RITH-roh-blas-toh-sis feh-TA-lis). Figure 11.14 illustrates the development of HDN.

❶ The mother is Rh-negative and is pregnant with an Rh-positive fetus.

❷ Fetal blood leaks through the placenta and mixes with the mother's blood. The mother becomes sensitized to the fetal Rh antigens and produces anti-Rh antibodies, which can cross the placenta into the fetal blood. The leakage of fetal blood is usually the result of a tear in the placenta that takes place either late in the pregnancy or during delivery. Thus, there is not sufficient time for the mother to produce enough anti-Rh antibodies to harm the fetus.

❸ In later pregnancies, however, a problem can arise because the mother has been sensitized to the Rh antigen.

❹ Consequently, if the fetus is Rh-positive and if any fetal blood leaks into the mother's blood, she rapidly produces large amounts of anti-Rh antibodies, which can cross the placenta to the fetus, resulting in HDN.

PROCESS Figure

Placenta
Fetal Rh-positive red blood cell in maternal circulation
Maternal blood
Placental tissue
Fetal blood in capillary
Fetal Rh-positive red blood cell
1
Maternal blood is separated from fetal blood by placental tissue.
First Pregnancy: Mother is Rh-negative and fetus is Rh-positive.
Anti-Rh antibodies
2
Maternal blood
3
4
Fetal blood in capillary
Subsequent Pregnancy: Fetus is Rh-positive.

PROCESS Figure 11.14 Hemolytic Disease of the Newborn (HDN)

Rh incompatibility may occur in a pregnancy when the mother is Rh-negative and the fetus is Rh-positive. The concern is usually for later pregnancies, after the mother has become sensitized to the Rh-antigen and is capable of producing anti-Rh antibodies at a faster and greater rate.

Explain why there is no concern for Rh incompatibilities in a pregnancy where the mother is Rh-positive and the fetus is Rh-negative.

Because HDN can be fatal to the fetus, the levels of anti-Rh antibodies in the mother's blood should be monitored. If they increase to unacceptable levels, the fetus should be tested to determine the severity of the HDN. In severe cases, a transfusion to replace lost red blood cells can be performed through the umbilical cord, or the baby can be delivered if mature enough.

Prevention of HDN is often possible if the Rh-negative mother is injected with a specific preparation called Rho(D) immune globulin (RhoGAM), which contains antibodies against Rh antigens. The injection can be given during the pregnancy, before delivery, or immediately after each delivery, miscarriage, or abortion. The injected antibodies bind to the Rh antigens of any fetal red blood cells that may have entered the mother's blood. This treatment inactivates the fetal Rh antigens and prevents sensitization of the mother.

Apply It 5

When treating HDN with an exchange transfusion, should the donor's blood be Rh-positive or Rh-negative? Explain.

11.7 DIAGNOSTIC BLOOD TESTS

Learning Outcome ***After reading this section, you should be able to***

A. Describe diagnostic blood tests and the normal values for the tests, and give examples of disorders that produce abnormal test values.

Type and Crossmatch

In today's medical settings, blood transfusions are common procedures that often are life-saving. To prevent transfusion reactions, the blood must be typed. **Blood typing** determines the ABO and Rh blood groups of a blood sample. Typically, the cells are separated from the plasma and then tested with known antibodies to determine the type of antigen on the cell surface. Agglutination during the typing procedure identifies the antigens on the red blood cells (figure 11.15). For example, if a patient's blood cells agglutinate when mixed with anti-A antibodies but do not agglutinate when mixed with anti-B antibodies, the cells have type A antigen. In a similar fashion, the serum is mixed with known cell types (antigens) to determine the type of antibodies in the serum.

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Figure 11.15 **Blood Typing**

Blood types are often determined by separating the blood cells from the plasma and then testing them with known antibodies. Agglutination, as seen in the middle and right-hand samples on the slide, indicates the presence of the antigen for the known antibody. Lack of agglutination, as seen in the left-hand sample on the slide, indicates that the antigen for the known antibody is not present.

Jarun011/iStock/Getty Images

Normally, donor blood must match the ABO and Rh type of the recipient. However, because other blood groups can cause a transfusion reaction, a crossmatch is performed. In a **crossmatch,** the donor's blood cells are mixed with the recipient's serum, and the donor's serum is

mixed with the recipient's cells. The donor's blood is considered safe for transfusion only if no agglutination occurs in either match.

Complete Blood Count

A **complete blood count (CBC)** is an analysis of blood that provides much useful information. A CBC consists of a red blood cell count, hemoglobin and hematocrit measurements, and a white blood cell count.

Red Blood Count

Blood cell counts are usually performed electronically with a machine, but they can also be done manually with a microscope. A normal **red blood count (RBC)** for a male is 4.6–6.2 million red blood cells per microliter (μL) of blood; for a female, a normal RBC count is 4.2–5.4 million per μL of blood. (A microliter is equivalent to 1 cubic millimeter [mm^3] or 10^{-6} L, and one drop of blood is approximately 50 μL.) The condition called **erythrocytosis** (eh-RITH-roh-sigh-TOH-sis) is an overabundance of red blood cells leading to increased blood viscosity, reduced flow rates and, if severe, plugged capillaries. See table 11.3 for details of the different types of erythrocytosis.

TABLE 11.3 REPRESENTATIVE DISEASES AND DISORDERS: Blood

Condition	Description
Erythrocytosis	
Relative erythrocytosis	Overabundance of red blood cells due to decreased blood volume, as may result from dehydration, diuretics, or burns
Primary erythrocytosis (polycythemia vera)	Stem cell defect of unknown cause; results in overproduction of red blood cells, granulocytes, and platelets; signs include low erythropoietin levels and enlarged spleen; increased blood viscosity and blood volume can cause clogging of the capillaries and hypertension
Secondary erythrocytosis	Overabundance of red blood cells resulting from decreased O_2 supply, as occurs at high altitudes, in chronic obstructive pulmonary disease, or in congestive heart failure; decreased O_2 delivery to the kidney stimulates the secretion of erythropoietin, resulting in increased blood viscosity and blood volume that can cause clogging of the capillaries and hypertension

Condition	Description
Clotting Disorders	
Disseminated intravascular coagulation (DIC)	Clotting throughout the vascular system, followed by bleeding; may develop when normal regulation of clotting by anticoagulants is overwhelmed, as occurs due to massive tissue damage; also caused by alteration of the lining of the blood vessels resulting from infections or snake bites
von Willebrand disease	Most common inherited bleeding disorder; platelet plug formation and the contribution of activated platelets to blood clotting are impaired; treatments are injection of von Willebrand factor or administration of drugs that increase von Willebrand factor levels in blood, which helps platelets adhere to collagen and become activated
Hemophilia	Genetic disorder in which clotting is abnormal or absent; each of the several types results from deficiency or dysfunction of a clotting factor; most often a sex-linked trait that occurs almost exclusively in males (see chapter 20)
Infectious Diseases of the Blood	
Septicemia (blood poisoning)	Spread of microorganisms and their toxins by the blood; often the result of a medical procedure, such as insertion of an intravenous tube; release of toxins by bacteria can cause septic shock, producing decreased blood pressure and possibly death
Malaria	Caused by a protozoan introduced into blood by the *Anopheles* mosquito; symptoms include chills and fever produced by toxins released when the protozoan causes red blood cells to rupture
Infectious mononucleosis	Caused by Epstein-Barr virus, which infects salivary glands and lymphocytes; symptoms include fever, sore throat, and swollen lymph nodes, all probably produced by the immune system response to infected lymphocytes
Acquired immunodeficiency syndrome (AIDS)	Caused by human immunodeficiency virus (HIV), which infects lymphocytes and suppresses immune system

Blood doping is an intentional process that serves to increase the number of circulating red blood cells. Having more red blood cells increases the blood's ability to transport O_2. Recall from chapter 7 that muscles require significant amounts of ATP for contraction, so increasing the O_2 supply to muscle tissue improves muscle performance, strength,

and endurance. Athletes have been known to use blood doping to enhance their performance. Blood doping can be accomplished in several ways, including the use of blood transfusions or by taking drugs that stimulate the process of red blood cell production. Though blood doping may sound harmless at first, the overall result is erythrocytosis—a very dangerous side effect.

Hemoglobin Measurement

The amount of hemoglobin in a given volume of blood is usually expressed in terms of grams of hemoglobin per 100 mL of blood. The normal hemoglobin measurement for a male is 14–18 grams (g) per 100 mL of blood, and for a female 12–16 g per 100 mL of blood. An abnormally low hemoglobin measurement is an indication of **anemia** (ah-NEE-mee-ah), which is either a reduced number of red blood cells or a reduced amount of hemoglobin in each red blood cell (see the Clinical Impact "Anemia" later in this chapter).

Hematocrit Measurement

The percentage of the total blood volume that is composed of red blood cells is the **hematocrit** (hee-MAT-oh-krit). One way to determine hematocrit is to place blood in a capillary tube and spin it in a centrifuge. The formed elements, which are heavier than the plasma, are forced to one end of the tube. Of these, the white blood cells and platelets form the buffy coat between the plasma and the red blood cells. The red blood cells account for 40–52% of the total blood volume in males and 38–48% in females. The hematocrit measurement is affected by the number and size of red blood cells because it is based on volume. For example, a decreased hematocrit can result from a decreased number of normal-size red blood cells or a normal number of small red blood cells. The average size of a red blood cell is calculated by dividing the hematocrit by the red blood cell count. A number of disorders cause red blood cells to be smaller or larger than normal. For example, inadequate iron in the diet can impair hemoglobin production. Consequently, red blood cells do not fill up with hemoglobin during their formation, and they remain smaller than normal.

CLINICAL IMPACT

Anemia

Anemia is a deficiency of normal hemoglobin in the blood, resulting from a decreased number of red blood cells, a decreased amount of hemoglobin in each red blood cell, or both. Anemia can also be caused by abnormal hemoglobin production.

Anemia reduces the blood's ability to transport O_2. People with anemia lack energy and feel excessively tired and listless. They may appear pale and become short of breath after only slight exertion.

One general cause of anemia is insufficient production of red blood cells. **Aplastic** (ay-PLAS-tik) **anemia** is caused by an inability of the red bone marrow to produce red blood cells and, often, white blood cells and platelets. It is usually acquired as a result of damage to the stem cells in red marrow by chemicals, such as benzene, certain antibiotics and sedatives, or radiation.

Red blood cell production can also be lower than normal due to nutritional deficiencies. **Iron-deficiency anemia** results from insufficient intake or absorption of iron or from excessive iron loss. Consequently, not enough hemoglobin is produced, the number of red blood cells decreases, and the red blood cells that are manufactured are smaller than normal.

Folate deficiency can also cause anemia. The usual cause of folate deficiency is inadequate folate in the diet. Because folate helps in the synthesis of DNA, a folate deficiency results in fewer cell divisions and therefore decreased red blood cell production.

Another type of nutritional anemia is **pernicious** (per-NISH-us) **anemia,** which is caused by inadequate vitamin B_{12}. Because vitamin B_{12} is important for folate synthesis, inadequate amounts of vitamin B_{12} can also result in decreased red blood cell production.

Another general cause of anemia is loss or destruction of red blood cells. **Hemorrhagic** (hem-oh-RAJ-ick) **anemia** results from a loss of blood due to trauma, ulcers, or excessive menstrual bleeding. Chronic blood loss, in which small amounts of blood are lost over a period of time, can cause iron-deficiency anemia. **Hemolytic** (hee-moh-LIT-ik) **anemia** occurs when red blood cells rupture or are destroyed at an excessive rate. It can be caused by inherited defects in the red blood cells. For example, one kind of inherited hemolytic anemia results from a defect in the cell membrane that causes red blood cells to rupture easily. Many kinds of hemolytic anemia result from unusual damage to the red blood cells by drugs, snake venom, artificial heart valves, autoimmune disease, or hemolytic disease of the newborn.

Anemia can also result from problems with the production of hemoglobin. **Thalassemia** (thal-ah-SEE-mee-ah) is a hereditary disease resulting in reduced rates of hemoglobin production. If hemoglobin production is severely depressed,

death usually occurs before age 20. In less severe cases, thalassemia produces a mild anemia.

Some anemias are caused by defective hemoglobin production. **Sickle-cell anemia** is a hereditary disease found mostly in people of African descent. The red blood cells assume a rigid sickle shape and plug up small blood vessels. They are also more fragile than normal. In severe cases, so much abnormal hemoglobin is produced that the disease is usually fatal before age 30. In many cases, however, enough normal hemoglobin is produced to compensate for the abnormal hemoglobin, and the person exhibits no symptoms.

White Blood Count

A **white blood count (WBC)** measures the total number of white blood cells in the blood. There are normally 5000–9000 white blood cells per microliter of blood. **Leukopenia** (loo-koh-PEE-nee-ah) is a lower than normal WBC resulting from decreased production or destruction of the red marrow. Radiation, drugs, tumors, viral infections, or a deficiency of the vitamins folate or B_{12} can cause leukopenia. **Leukocytosis** (LOO-koh-sigh-TOH-sis) is an abnormally high WBC. Bacterial infections often cause leukocytosis by stimulating neutrophils to increase in number. **Leukemia** (loo-KEE-mee-ah), cancer of the red marrow characterized by abnormal production of one or more of the white blood cell types, can cause leukocytosis. However, the white blood cells do not function normally. Because these cells are usually immature or abnormal and lack normal immunological functions, people with leukemia are very susceptible to infections. The excess production of white blood cells in the red marrow can also interfere with the formation of red blood cells and platelets and thus lead to anemia and bleeding.

Differential White Blood Count

A **differential white blood count** determines the percentage of each of the five kinds of white blood cells. Normally, neutrophils account for 60–70%, lymphocytes 20–25%, monocytes 3–8%, eosinophils 2–4%, and basophils 0.5–1% of all white blood cells. Much insight into a patient's condition can be obtained from a differential white blood count. For example, if a bacterial infection is present, the neutrophil count is often greatly increased, whereas in allergic reactions, the eosinophil and basophil counts are elevated.

Clotting

There are two common ways to measure the blood's ability to clot: platelet count and prothrombin time measurement.

Platelet Count

A normal **platelet count** is 250,000–400,000 platelets per microliter of blood. In the condition called **thrombocytopenia** (THROM-boh-sigh-toh-PEE-nee-ah), the platelet count is greatly reduced, resulting in chronic bleeding through small vessels and capillaries. It can be caused by decreased platelet production as a result of hereditary disorders, lack of vitamin B_{12} (pernicious anemia), drug therapy, or radiation therapy.

Prothrombin Time Measurement

Prothrombin time measurement calculates how long it takes for the blood to start clotting, which is normally 9–12 seconds. Prothrombin time is determined by adding thromboplastin to whole plasma. Thromboplastin is a chemical released from injured tissues that starts the process of clotting (see figure 11.10). Prothrombin time is officially reported as the International Normalized Ratio (INR), which standardizes the time it takes to clot on the basis of the slightly different thromboplastins used by different labs. Because many clotting factors have to be activated to form fibrin, a deficiency of any one of them can cause the prothrombin time to be abnormal. Vitamin K deficiency, certain liver diseases, and drug therapy can increase prothrombin time.

Blood Chemistry

The composition of materials dissolved or suspended in the plasma can be used to assess the functioning of many of the body's systems. For example, high blood glucose levels can indicate that the pancreas is not producing enough insulin; high blood urea nitrogen (BUN) is a sign of reduced kidney function; increased bilirubin can indicate liver dysfunction; and high cholesterol levels can signify an increased risk of cardiovascular disease. A number of blood chemistry tests are routinely done when a blood sample is taken, and additional tests are available.

Apply It 6

When a patient complains of acute pain in the abdomen, the physician suspects appendicitis, a bacterial infection of the appendix. What blood test can provide supporting evidence for that diagnosis?

SUMMARY

11.1 Functions of Blood

1. Blood transports gases, nutrients, waste products, processed molecules, and regulatory molecules.
2. Blood regulates pH as well as fluid and ion balance.
3. Blood is involved with temperature regulation and protects against foreign substances, such as microorganisms and toxins.
4. Blood clotting prevents fluid and cell loss and is part of tissue repair.

11.2 Composition of Blood

1. Blood is a connective tissue consisting of plasma and formed elements.
2. Total blood volume in an average adult is approximately 5 L.

11.3 Plasma

1. Plasma is 91% water and 9% suspended or dissolved substances.
2. Plasma maintains osmotic pressure, is involved in immunity, prevents blood loss, and transports molecules.

11.4 Formed Elements

The formed elements are cells (red blood cells and white blood cells) and cell fragments (platelets).

Production of Formed Elements

Formed elements arise (hematopoiesis) in red bone marrow from hematopoietic stem cells.

Red Blood Cells

1. Red blood cells are disk-shaped cells containing hemoglobin, which transports O_2 and CO_2. Red blood cells also contain carbonic anhydrase, which is involved with carbon dioxide transport.
2. In response to low blood O_2 levels, the kidneys produce erythropoietin, which stimulates red blood cell production in red bone marrow.
3. Worn-out red blood cells are phagocytized by macrophages in the spleen or liver. Hemoglobin is broken down, iron and amino acids are reused, and heme becomes bilirubin that is secreted in bile.

White Blood Cells

1. White blood cells protect the body against microorganisms and remove dead cells and debris.
2. Granulocytes contain cytoplasmic granules. The three types of granulocytes are neutrophils, small phagocytic cells; basophils, which promote inflammation; and eosinophils, which defend against parasitic worms and influence inflammation.
3. Agranulocytes have very small granules and are of two types: Lymphocytes are involved in antibody production and other immune system responses; monocytes become macrophages that ingest microorganisms and cellular debris.

Platelets

Platelets are cell fragments involved with preventing blood loss.

11.5 Preventing Blood Loss

Vascular Spasm

Blood vessels constrict in response to injury, resulting in decreased blood flow.

Platelet Plug Formation

1. Platelet plugs repair minor damage to blood vessels.

2. Platelet plugs form when platelets adhere to collagen, release chemicals (ADP and thromboxanes) that activate other platelets, and connect to one another with fibrinogen.

Blood Clotting

1. Blood clotting, or coagulation, is the formation of a clot (a network of protein fibers called fibrin).
2. There are three steps in the clotting process: (1) activation of clotting factors by connective tissue and chemicals, resulting in the formation of prothrombinase; (2) conversion of prothrombin to thrombin by prothrombinase; and (3) conversion of fibrinogen to fibrin by thrombin.
3. Anticoagulants in the blood, such as antithrombin and heparin, prevent clot formation.
4. Clot retraction condenses the clot, pulling the edges of damaged tissue closer together.
5. Serum is plasma without clotting factors.
6. Fibrinolysis (clot breakdown) is accomplished by plasmin.

11.6 Blood Grouping

1. Blood groups are determined by antigens on the surface of red blood cells.
2. In transfusion reactions, antibodies can bind to red blood cell antigens, resulting in agglutination or hemolysis of red blood cells.

ABO Blood Group

1. Type A blood has A antigens, type B blood has B antigens, type AB blood has A and B antigens, and type O blood has neither A nor B antigens.
2. Type A blood has anti-B antibodies, type B blood has anti-A antibodies, type AB blood has neither anti-A nor anti-B antibodies, and type O blood has both anti-A and anti-B antibodies.
3. Mismatching the ABO blood group can result in transfusion reactions.

Rh Blood Group

1. Rh-positive blood has Rh antigens, whereas Rh-negative blood does not.
2. Antibodies against the Rh antigen are produced when an Rh-negative person is exposed to Rh-positive blood.
3. The Rh blood group is responsible for hemolytic disease of the newborn, which can occur when the fetus is Rh-positive and the mother is Rh-negative.

11.7 Diagnostic Blood Tests

Type and Crossmatch

1. Blood typing determines the ABO and Rh blood groups of a blood sample.
2. A crossmatch tests for agglutination reactions between donor and recipient blood.

Complete Blood Count

The complete blood count consists of the red blood count (million/μL), the hemoglobin measurement (grams of hemoglobin per 100 mL of blood), the hematocrit measurement (percent volume of red blood cells), and the white blood count (million/μL).

Differential White Blood Count

The differential white blood count determines the percentage of each type of white blood cell.

Clotting

Platelet count and prothrombin time measurement determine the blood's ability to clot.

Blood Chemistry

The composition of materials dissolved or suspended in plasma (e.g., glucose, urea nitrogen, bilirubin, and cholesterol) can be used to assess the functioning and status of the body's systems.

REMEMBERING AND UNDERSTANDING

1. Describe the functions of blood.
2. Define plasma, and list its functions.
3. Define formed elements, and name the different types of formed elements. Explain how and where the formed elements arise through hematopoiesis.
4. Describe the two basic parts of a hemoglobin molecule. Which part is associated with iron? What gases are transported by each part?
5. What is the role of carbonic anhydrase in gas transport?
6. Why are the vitamins folate and B_{12} important in red blood cell production?
7. Explain how low blood O_2 levels result in increased red blood cell production.
8. Where are red blood cells broken down? What happens to the breakdown products?
9. Give two functions of white blood cells.
10. Name the five types of white blood cells, and state a function for each type.
11. What are platelets, and how are they formed?
12. Describe the role of blood vessel constriction and platelet plugs in preventing bleeding. Describe the three steps of platelet plug formation.
13. What are clotting factors? Describe the three steps of activation that result in the formation of a clot.

14. Explain the function of anticoagulants in the blood, and give an example of an anticoagulant.
15. What is clot retraction, and what does it accomplish?
16. Define fibrinolysis, and name the chemicals responsible for this process.

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17. What are blood groups, and how do they cause transfusion reactions? List the four ABO blood types. Why is a person with type O blood considered a universal donor?
18. What is meant by the term *Rh-positive?* How can Rh incompatibility affect a pregnancy?
19. For each of the following tests, define the test and give an example of a disorder that would cause an abnormal test result:
    a. type and crossmatch
    b. red blood count
    c. hemoglobin measurement
    d. hematocrit measurement
    e. white blood count
    f. differential white blood count
    g. platelet count
    h. prothrombin time
    i. blood chemistry

CRITICAL THINKING

1. Jackson, a physical education major, wanted to improve his performance in an upcoming marathon. About 6 weeks before the race, he had 1 L of blood removed from his body and the formed elements separated from the plasma. The formed elements were frozen, and the plasma was reinfused

into his body. Just before the race, the formed elements were thawed and injected into his circulatory system. Explain why this procedure, called blood doping or blood boosting, would help Jackson's performance. Can you suggest any possible bad effects?

2. Chemicals such as benzene can destroy red bone marrow, causing aplastic anemia. What symptoms would you expect as a result of the lack of (a) red blood cells, (b) platelets, and (c) white blood cells?
3. Robert habitually used barbiturates to ease feelings of anxiety. Because barbiturates depress the respiratory centers in the brain, they cause hypoventilation (i.e., a slower than normal breathing rate). What happens to the red blood cell count of a habitual user of barbiturates? Explain.
4. What blood problems would you expect in a patient after a total gastrectomy (removal of the stomach)?
5. According to an old saying, "Good food makes good blood." Name three substances in the diet that are essential for "good blood." What blood disorders develop if these substances are absent from the diet?
6. Shaina has a cell membrane defect in her red blood cells that makes them more susceptible to rupture. Her red blood cells are destroyed faster than they can be replaced. Would her RBC, hemoglobin, hematocrit, and bilirubin levels be below normal, normal, or above normal? Explain.

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

12

Heart

The heart is a four-chambered muscular organ that pumps blood through the blood vessels of the body. The wall of the heart is composed of three layers of tissue, including a middle layer of cardiac muscle. The heart is surrounded by the pericardium, which anchors the heart in the mediastinum.

LEARN TO APPLY IT

Grandpa Stan never missed his grandson's baseball games. One day, while climbing into the bleachers, he had difficulty breathing and knew he'd better see a doctor. Using a stethoscope, Stan's regular physician could hear an irregular swooshing after the first heart sound, so he referred Stan to a cardiologist. The cardiologist conducted a series of exams and determined that Stan has an incompetent bicuspid valve.

After reading this chapter, identify the major functional changes in the heart that result from an incompetent valve, and explain how these changes led to Stan's symptoms.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 9 Cardiovascular System

12.1 FUNCTIONS OF THE HEART

Learning Outcome ***After reading this section, you should be able to***

A. List the major functions of the heart.

People often refer to the heart as the seat of strong emotions. For example, we may describe a very determined person as having "a lot of heart" or say that a person who has been disappointed romantically has a "broken heart." Emotions, however, are a product of brain function, not heart function. The heart is a muscular organ that is essential for life because it pumps blood through the body.

Fluids flow through a pipe only if they are forced to do so. The force is commonly produced by a pump, which increases the pressure of the liquid at the pump above the pressure in the pipe. Thus, the liquid flows from the pump through the pipe from an area of higher pressure to an area of lower pressure. If the pressure produced by the pump increases, flow of liquid through the pipe increases. If the pressure produced by the pump decreases, flow of liquid through the pipe decreases.

Like a pump that forces water through a pipe, the heart contracts forcefully to pump blood through the blood vessels of the body. Together, the heart, the blood vessels, and the blood make up the **cardiovascular system** (figure 12.1). The heart of a healthy adult, at rest, pumps

approximately 5 liters (L) of blood per minute. For most people, the heart continues to pump at approximately that rate for more than 75 years. During short periods of vigorous exercise, the amount of blood pumped per minute increases several-fold. But if the heart loses its pumping ability for even a few minutes, blood flow through the blood vessels stops, and the person's life is in danger.

Figure 12.1 APR **Cardiovascular System**
The heart, the blood vessels, and the blood are the major components of the cardiovascular system.

Although it is a single structure, the heart is actually two pumps in one. The right side of the heart pumps blood to the lungs and back to the left side of the heart through vessels of the **pulmonary circulation** (figure 12.2). The left side of the heart pumps blood to all other tissues of the body and back to the right side of the heart through vessels of the **systemic circulation.**

Figure 12.2 APR **Overview of the Circulatory System**

The circulatory system consists of the pulmonary and systemic circulations. The right side of the heart pumps blood through vessels to the lungs and back to the left side of the heart through the pulmonary circulation. The left side of the heart pumps blood through vessels to the body tissues and back to the right side of the heart through the systemic circulation.

The functions of the heart are

1. *Generating blood pressure*. Contractions of the heart generate blood pressure, which forces blood through the blood vessels.
2. *Routing blood*. The heart separates the pulmonary and systemic circulations, which ensures that the blood flowing to tissues has adequate levels of O_2.
3. *Ensuring one-way blood flow*. The valves of the heart ensure a one-way flow of blood through the heart and blood vessels.
4. *Regulating blood supply*. Changes in the rate and force of heart contraction match blood flow to the changing metabolic needs of the tissues during rest, exercise, and changes in body position.

12.2 SIZE, FORM, AND LOCATION OF THE HEART

Learning Outcomes *After reading this section, you should be able to*

A. Describe the size, shape, and location of the heart.

B. Explain why knowing the heart's location is important.

The adult heart is shaped like a blunt cone and is approximately the size of a closed fist. It is larger in physically active adults than in less active but otherwise healthy adults. The heart generally decreases in size after approximately age 65, especially in people who are not physically active. The blunt, rounded point of the heart is the **apex** and the larger, flat part at the opposite end of the heart is the **base.**

The heart is located in the thoracic cavity between the two pleural cavities that surround the lungs. The heart, trachea, esophagus, and associated structures form a midline partition called the **mediastinum** (MEE-dee-ah-STIE-num; see figure 1.11). The heart is surrounded by its own cavity, the **pericardial cavity** (*peri,* around + *cardio,* heart) (see chapter 1).

It is important for health professionals to know the location and shape of the heart in the thoracic cavity. This knowledge enables them to accurately place a stethoscope to hear the heart sounds, to place chest leads for an electrocardiogram (described later in this chapter), or to administer **cardiopulmonary resuscitation** (KAR-dee-oh-PUL-moh-nair-ee ree-SUS-ih-TAY-shun; **CPR)**. CPR is an emergency procedure that maintains blood flow in the body if a person's heart stops.

The heart lies obliquely (at an angle) in the mediastinum, with its base directed posteriorly and slightly superiorly and its apex directed anteriorly and slightly inferiorly. The apex is also directed to the left, so that approximately two-thirds of the heart's mass lies to the left of the midline of the sternum (figure 12.3*a*). The base of the heart is located just behind the sternum and extends to the space just below the second rib, called the second intercostal space. The apex is just behind the 5th and 6th ribs at the 5th intercostal space and just to the left of the sternum. If you draw an imaginary line straight down from the middle of your left clavicle, it will pass over the apex. This perpendicular line is called the midclavicular line (figure 12.3*b*).

Figure 12.3 APR **Location of the Heart**

(*a*) The heart is in the thoracic cavity between the lungs, deep and slightly to the left of the sternum. (*b*) The base of the heart, located deep to the sternum, extends superiorly to the second intercostal space, and the apex of the heart is located deep to the fifth intercostal space, approximately 7–9 cm to the left of the sternum where the midclavicular line intersects with the fifth intercostal space.

12.3 ANATOMY OF THE HEART

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the structure of the pericardium.
B. Give the location and function of the coronary arteries.
C. Describe the chambers of the heart.
D. Name the valves of the heart, and state their locations and functions.
E. Describe the flow of blood through the heart, and name each of the chambers and structures through which the blood passes.

Pericardium

The heart lies in the **pericardial cavity.** The pericardial cavity is formed by the **pericardium** (per-ih-KAR-dee-um), or *pericardial sac,* which surrounds the heart and anchors it within the mediastinum (figure 12.4). The pericardium consists of two layers: (1) the fibrous pericardium and (2) the serous pericardium. The **fibrous pericardium** is the outer layer of the pericardium and is composed of tough, fibrous connective tissue. The

serous pericardium is the inner layer and consists of flat epithelial cells with a thin layer of connective tissue. The serous pericardium, like most serous membranes, is composed of two parts: (1) the parietal pericardium and (2) the visceral pericardium. The **parietal pericardium** lines the fibrous pericardium, whereas the **visceral pericardium,** or *epicardium* (EP-ih-KAR-dee-um; upon the heart) covers the heart surface. The parietal and visceral pericardia are continuous with each other where the great vessels enter or leave the heart. The pericardial cavity, located between the visceral and parietal pericardia, is filled with a thin layer of **pericardial fluid** produced by the serous pericardium. The pericardial fluid helps reduce friction as the heart moves within the pericardium.

Figure 12.4 APR **Heart in the Pericardium**

The pericardium consists of an outer fibrous pericardium and an inner serous pericardium. The serous pericardium has two parts: The parietal pericardium lines the fibrous pericardium, and the visceral pericardium (epicardium) covers the surface of the heart. The pericardial cavity, between the parietal pericardium and visceral pericardium, is filled with a small amount of pericardial fluid.

CLINICAL IMPACT

Disorders of the Pericardium

Pericarditis (PER-i-kar-DYE-tis) is an inflammation of the serous pericardium. The cause is frequently unknown, but it can result from infection, diseases of connective tissue, or damage due to radiation treatment for cancer. The condition can cause extremely painful sensations that are referred to the back and to the chest and can be confused with a myocardial infarction (heart attack). Pericarditis can lead to a small amount of fluid accumulation within the pericardial sac.

Cardiac tamponade (tam-puh-NAYD; a pack or plug) is a potentially fatal condition in which fluid or blood accumulates in the pericardial cavity and compresses the heart from the outside. The heart is a powerful muscle, but it relaxes passively. When it is compressed by fluid within the pericardial cavity, it cannot expand when the cardiac muscle relaxes. Consequently, the heart cannot fill with blood during relaxation, which makes pumping impossible. Cardiac tamponade can cause a person to die quickly unless the fluid is removed. Causes of cardiac tamponade include rupture of the heart wall following a myocardial infarction, rupture of blood vessels in the pericardium after a malignant tumor invades the area, damage to the pericardium due to radiation therapy, and trauma, such as that resulting from a traffic accident.

External Anatomy

The right and left **atria** (AY-tree-ah; sing. atrium, entrance chamber) are located at the base of the heart, and the right and left **ventricles** (VEN-trih-kels; cavities) extend from the base of the heart toward the apex (figure 12.5). A groove called the **coronary sulcus** (SUL-cuss) extends around the heart, separating the atria from the ventricles. Two additional grooves, or sulci extend inferiorly from the coronary sulcus and indicate the division between the right and left ventricles. The **anterior interventricular sulcus** is on the anterior surface of the heart, and the **posterior interventricular sulcus** is on the posterior surface of the heart.

(a) **Anterior view**

Anterior view

(b)

Figure 12.5 APR **Surface of the Heart**

(*a*) In this anterior view of the heart, the two atria (right and left) are located superiorly at the base of the heart, and the two ventricles (right and left) are located inferiorly at the apex of the heart. The superior and inferior venae cavae enter the right atrium. The pulmonary veins enter the left atrium. The pulmonary trunk exits the right ventricle, and the aorta exits the left ventricle. (*b*) Photograph of the anterior surface of the heart.

(b) ©R. T. Hutchings

(c) Posterior view of the heart.

Blood first enters the heart at the atria. Veins carry blood to the atria (figure 12.5*a, c*): The **superior vena cava** and **inferior vena cava** carry blood from the body to the right atrium, and four **pulmonary veins** carry blood from the lungs to the left atrium. Blood exits the heart at the ventricles. Blood flows from the ventricles through large arteries, often called the great vessels or great arteries. The **pulmonary trunk,** arising from the right ventricle, splits into the right and left **pulmonary arteries,** which carry blood to the lungs. The **aorta** (ay-OR-tuh), arising from the left ventricle, carries blood to the rest of the body.

Heart Chambers and Internal Anatomy

The heart is a muscular pump consisting of four chambers: (1) the right atrium, (2) the left atrium, (3) the right ventricle, and (4) the left ventricle (figure 12.6).

Figure 12.6 APR **Internal Anatomy of the Heart**
The heart is cut in a frontal plane to show its internal anatomy.

Right and Left Atria

Blood enters the atria of the heart through blood vessels called veins. The atria function primarily as reservoirs, where blood returning from veins collects before it enters the ventricles. Contraction of the atria forces blood into the ventricles to complete ventricular filling. The right atrium receives blood from three major openings: (1) the superior vena cava, (2) the inferior vena cava, and (3) the coronary sinus. The superior vena cava and the inferior vena cava drain blood from most of the body (figure 12.6), and the smaller coronary sinus drains blood from most of the heart muscle. The left atrium receives blood through the four pulmonary veins, which drain blood from the lungs. The two atria are separated from each other by a partition called the **interatrial** (between the atria) **septum.**

Right and Left Ventricles

The ventricles of the heart are its major pumping chambers. They eject blood into the arteries and force it to flow through the circulatory system. The atria open into the ventricles, and each ventricle has one large outflow route located superiorly near the midline of the heart. The right ventricle pumps blood into the pulmonary trunk, and the left ventricle pumps blood

into the aorta. The two ventricles are separated from each other by the muscular **interventricular** (between the ventricles) **septum** (figure 12.6).

The wall of the left ventricle is thicker than the wall of the right ventricle. As such, the wall of the left ventricle contracts more forcefully and generates a greater blood pressure than the wall of the right ventricle. When the left ventricle contracts, the pressure increases to approximately 120 mm Hg. When the right ventricle contracts, the pressure increases to approximately 24 mm Hg or one-fifth of the pressure in the left ventricle. However, the left and right ventricles pump nearly the same volume of blood. The higher pressure generated by the left ventricle moves blood through the larger systemic circulation, whereas the lower pressure generated by the right ventricle moves blood through the smaller pulmonary circulation (see figure 12.2).

Heart Valves

The one-way flow of blood through the heart chambers is maintained by the heart valves. There are two types of heart valves: (1) atrioventricular valves and (2) semilunar valves. An **atrioventricular (AV) valve** is located between each atrium and ventricle. Specifically, the AV valve between the right atrium and the right ventricle is called the **tricuspid valve** (figure 12.7*a*), because it is composed of three cusps or flaps of tissue. The AV valve between the left atrium and the left ventricle is called the **bicuspid valve,** because it is composed of two cusps. The bicuspid valve is also called the *mitral* (resembling a bishop's miter, a two-pointed hat) *valve* (figure 12.7*b*). These valves allow blood to flow from the atria into the ventricles but prevent it from flowing back into the atria. When the ventricles relax, the higher pressure in the atria forces the AV valves to open, and blood flows from the atria into the ventricles (figure 12.8*a*). In contrast, when the ventricles contract, blood flows toward the atria and causes the AV valves to close (figure 12.8*b*). This information may be useful in answering the Learn to Apply It question at the beginning of the chapter.

Figure 12.7 APR **Heart Valves**

(*a*) Anterior view of the tricuspid valve, bicuspid valve, the chordae tendineae, and the papillary muscles. (*b*) In superior view, note that the three cusps of each semilunar valve meet to prevent the backflow of blood.

(a) ©Oktay Ortakcioglu/iStock/360/Getty Images RF; (b) ©VideoSurgery/Science Source;

Figure 12.8 APR **Function of the Heart Valves**

(*a*) As the ventricle relaxes, the pressure in the ventricle becomes lower than the pressure in the atrium. Blood flowing into the left atrium opens the bicuspid valve, and blood flows into the left ventricle. At the same time, in the aorta, blood flowing back toward the relaxed ventricle causes the aortic semilunar valve to close, and no blood can reenter the ventricle from the aorta. (*b*) When the ventricle contracts, blood flowing toward the atrium causes the bicuspid valve to close. The increased pressure in the left ventricle forces the aortic semilunar valve open.

Each ventricle contains cone-shaped, muscular pillars called **papillary** (PAP-i-lar-ee) **muscles.** These muscles are attached by thin, strong,

connective tissue strings called **chordae tendineae** (KOR-dee ten-DIN-ee; heart strings) to the free margins of the cusps of the atrioventricular valves. When the ventricles contract, the papillary muscles contract and prevent the valves from opening into the atria by pulling on the chordae tendineae attached to the valve cusps (see figures 12.6 and 12.7*a*; figure 12.8). Imagine a parachute billowing open, with the parachute cords securing its shape. The parachute fabric is analogous to the cusps of the valves and the parachute cords are analogous to the chordae tendineae.

A **semilunar valve** is located between each ventricle and its associated great artery. The **pulmonary semilunar valve** is located between the right ventricle and the pulmonary trunk. The **aortic semilunar valve** is located between the left ventricle and aorta (see figure 12.6). Each valve consists of three pocketlike semilunar (half-moon-shaped) cusps (see figure 12.7*b*; figure 12.8). When the ventricles relax, the pressures in the aorta and pulmonary trunk are higher than in the ventricles. Blood flows back from the aorta or pulmonary trunk toward the ventricles and enters the pockets of the cusps, causing them to bulge toward and meet in the center of the aorta or pulmonary trunk, thus closing the vessels and blocking blood flow back into the ventricles (figure 12.8*a*). When the ventricles contract, the increasing pressure within the ventricles forces the semilunar valves to open (figure 12.8*b*).

A plate of connective tissue, sometimes called the **cardiac skeleton,** or fibrous skeleton, consists mainly of fibrous rings that surround the atrioventricular and semilunar valves and give them solid support (figure 12.9). This connective tissue plate also serves as electrical insulation between the atria and the ventricles and provides a rigid attachment site for cardiac muscle.

Figure 12.9 **Cardiac Skeleton**

The cardiac skeleton consists of fibrous connective tissue rings that surround the heart valves and separate the atria from the ventricles. Cardiac muscle attaches to the fibrous connective tissue. The muscle fibers are arranged so that, when the ventricles contract, a wringing motion is produced, and the distance between the apex and the base of the heart shortens.

Route of Blood Flow Through the Heart

The route of blood flow through the heart is depicted in figure 12.10. Even though blood flow is described for the right and then the left side of the heart, it is important to understand that both atria contract at the same time, and both ventricles contract at the same time. This concept is most important when considering the electrical activity, pressure changes, and heart sounds.

1. Deoxygenated blood enters the right atrium from the systemic circulation through the superior and inferior venae cavae, and from heart muscle through the coronary sinus.
2. Most of the blood flowing into the right atrium flows through the tricuspid valve and into the relaxed right ventricle. Before the end of ventricular relaxation, the right atrium contracts, and enough blood is pushed from the right atrium into the right ventricle to complete right ventricular filling.
3. Following right atrial contraction, the right ventricle begins to contract. This contraction pushes blood against the tricuspid valve, forcing it closed. After pressure within the right ventricle increases, the

pulmonary semilunar valve is forced open, and blood flows into the pulmonary trunk. As the right ventricle relaxes, its pressure falls rapidly, and pressure in the pulmonary trunk becomes greater than in the right ventricle. The backflow of blood forces the pulmonary semilunar valve to close.

4. The pulmonary trunk branches to form the right and left pulmonary arteries, which carry blood to the lungs, where CO_2 is released and O_2 is picked up.
5. Oxygenated blood returning from the lungs enters the left atrium through the four pulmonary veins.
6. Most of the blood flowing into the left atrium passes through the bicuspid valve and into the relaxed left ventricle. Before the end of ventricular relaxation, the left atrium contracts, and enough blood is pushed from the left atrium into the left ventricle to complete left ventricular filling.
7. Following left atrial contraction, the left ventricle begins to contract. This contraction pushes blood against the bicuspid valve, forcing it closed. After pressure within the left ventricle increases, the aortic semilunar valve is forced open, and blood flows into the aorta.
8. Blood flowing through the aorta is distributed to all parts of the body, except to those parts of the lungs supplied by the pulmonary blood vessels. As the left ventricle relaxes, its pressure falls rapidly, and pressure in the aorta becomes greater than in the left ventricle. The backflow of blood forces the aortic semilunar valve to close.

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PROCESS Figure

PROCESS Figure 12.10 APR Blood Flow Through the Heart

(*a*) Frontal section of the heart, revealing the four chambers and the direction of blood flow (*purple numbers*). (*b*) Diagram listing in order the structures through which blood flows in the systemic and pulmonary circulations. The heart valves are indicated by *circles,* deoxygenated blood by *blue*, and oxygenated blood by *red.*

Imagine that you are a red blood cell moving through the circulation. After moving into the right atrium, how many heart valves will you pass through before you enter the circulation of the lungs? How many heart valves will you pass through before entering the circulation of the brain?

Blood Supply to the Heart

Coronary Arteries

The cardiac muscle in the wall of the heart is thick and metabolically very active and therefore requires an ample blood supply. Coronary arteries and cardiac veins provide the pathway for blood through the heart wall. Two **coronary arteries** supply blood to the wall of the heart (figure 12.11*a*). The coronary arteries originate from the base of the aorta, just above the aortic semilunar valves. The **left coronary artery** originates on the left side of the aorta. It has three major branches: (1) the anterior interventricular artery, (2) the circumflex artery, and (3) the left marginal artery. The **anterior interventricular artery** lies in the anterior interventricular sulcus; the **circumflex artery** extends around the coronary sulcus on the left to the posterior surface of the heart; and the **left marginal artery** extends inferiorly along the lateral wall of the left ventricle from the circumflex artery. The branches of the left coronary artery supply much of the anterior wall of the heart and most of the left ventricle.

Figure 12.11 APR **Blood Supply to the Heart**

The vessels of the anterior surface of the heart depicted here are darker in color, whereas the vessels of the posterior surface are seen through the heart and are lighter in color. (*a*) Coronary arteries supply blood to the wall of the heart. (*b*) Cardiac veins carry blood from the wall of the heart back to the right atrium.

The **right coronary artery** originates on the right side of the aorta. It extends around the coronary sulcus on the right to the posterior surface of the heart and gives rise to the **posterior interventricular artery,** which lies in the posterior interventricular sulcus. The **right marginal artery** extends inferiorly along the lateral wall of the right ventricle. The right coronary artery and its branches supply most of the wall of the right ventricle.

In a resting person, blood flowing through the coronary arteries gives up approximately 70% of its O_2. In comparison, blood flowing through arteries to skeletal muscle gives up only about 25% of its O_2. The percentage of O_2 the blood releases to skeletal muscle increases to 70% or more during exercise, but the percentage of O_2 the blood releases to cardiac muscle cannot increase substantially during exercise. Therefore, the rate of blood flow through the coronary arteries must increase above its resting level to provide cardiac muscle with adequate O_2 during exercise. When the heart contracts, the blood vessels of the coronary circulation are compressed, reducing blood flow through them. As a consequence, blood flow into the coronary circulation is greatest while the ventricles of the heart are relaxed. This is different compared to blood vessels in other tissues because blood

flow into other arteries of the body is highest during contraction of the ventricles.

Apply It 1

Describe the effect on the heart if blood flow through the anterior interventricular artery is restricted or completely blocked (Hint: See figure 12.11a).

Cardiac Veins

The **cardiac veins** drain blood from the cardiac muscle. Their pathways are nearly parallel to the coronary arteries, and most of them drain blood into the **coronary sinus,** a large vein located within the coronary sulcus on the posterior aspect of the heart. Blood flows from the coronary sinus into the right atrium (figure 12.11*b*). Some small cardiac veins drain directly into the right atrium.

12.4 HISTOLOGY OF THE HEART

Learning Outcomes *After reading this section, you should be able to*

A. List the components of the heart wall, and describe the structure and function of each.

B. Describe the structural and functional characteristics of cardiac muscle cells.

Heart Wall

The heart wall is composed of three layers of tissue: (1) the epicardium, (2) the myocardium, and (3) the endocardium (figure 12.12). The **epicardium** (EP-ih-KAR-dee-um), also called the *visceral pericardium,* is a thin, serous membrane forming the smooth outer surface of the heart. It consists of simple squamous epithelium overlying a layer of loose connective tissue and adipose tissue. The **myocardium** (MY-oh-KAR-dee-um) is the thick, middle layer of the heart, composed of cardiac muscle cells. The myocardium is responsible for contraction of the heart chambers. The **endocardium** (EN-doh-KAR-dee-um) is the smooth inner surface of the heart, which consists of simple squamous epithelium over a layer of connective tissue. The endocardium allows blood to move easily through the heart. The heart valves are formed by folds of endocardium that include a thick layer of connective tissue.

Figure 12.12 **Heart Wall**

This enlarged section of the heart wall illustrates the epicardium (visceral pericardium), the myocardium, and the endocardium.

The surfaces of the interior walls of the ventricles are modified by ridges and columns of cardiac muscle called **trabeculae carneae.** Smaller muscular ridges are also present in portions of the atria.

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CLINICAL IMPACT

Heart Attack

When a blood clot, or **thrombus** (THROM-bus; a clot), suddenly blocks a coronary blood vessel, a **heart attack,** or *coronary thrombosis* (throm-BOH-sis), occurs. The area that has been cut off from its blood supply suffers from lack of O_2 and nutrients and dies if the blood supply is not quickly reestablished. The region of dead heart tissue is called an **infarct** (in-FARKT), or *myocardial infarction.* If the infarct is large, the heart may be unable to pump enough blood to keep the person alive. People can reduce their risk of having a heart attack by taking small amounts of aspirin daily, which inhibits thrombus formation (see chapter 11).

Aspirin is also administered to many people who are exhibiting clear symptoms of a heart attack. In some cases, it is possible to treat heart attacks with enzymes, such as **tissue plasminogen** (plaz-MIN-oh-jen) **activator (t-PA),** which break down blood clots. One of the enzymes is injected into the circulatory system of a heart attack patient, where it reduces or removes the blockage in the coronary artery. If the clot is broken down quickly, the blood supply to cardiac muscle is reestablished, and the heart may suffer little permanent damage.

Coronary arteries can become blocked more gradually by **atherosclerotic** (ah-ther-oh-skleh-ROE-sis; *athero,* pasty material + *sclerosis,* hardness) **plaque.** These thickenings in the walls of arteries can contain deposits that are high in cholesterol and other lipids. The lesions narrow the lumen (opening) of the arteries, thus restricting blood flow. The ability of cardiac muscle to function is reduced when it is deprived of an adequate blood supply. The person suffers from fatigue and often experiences pain in the area of the chest and usually in the left arm with the slightest exertion. The pain is called **angina pectoris** (an-JYE-na, pain; PEK-toh-ris, in the chest).

Angioplasty (AN-jee-oh-PLAS-tee) is a procedure in which a surgeon threads a small balloon through the aorta and into a coronary artery. After entering a partially blocked coronary artery, the balloon is inflated, flattening the atherosclerotic deposits against the vessel wall and opening the blocked blood vessel. This technique improves the function of cardiac muscle in patients experiencing inadequate blood flow to the cardiac muscle through the coronary arteries. Some controversy exists about its effectiveness, at least in some patients, because dilation of the coronary arteries can be reversed within a few weeks or months and because blood clots can form in coronary arteries following angioplasty. Small rotating blades and lasers are also used to remove lesions from coronary vessels, or a small coil device, called a **stent,** may be placed in a vessel to hold it open following angioplasty.

A **coronary bypass** is a surgical procedure that relieves the effects of obstructions in the coronary arteries. The technique involves taking healthy segments of blood vessels from other parts of the patient's body and using them to bypass, or create an alternative path around, obstructions in the coronary arteries. The technique is common in cases of severe blockage of parts of the coronary arteries.

Cardiac Muscle

Cardiac muscle cells are elongated, branching cells that contain one, or occasionally two, centrally located nuclei (figure 12.13). Cardiac muscle cells contain actin and myosin myofilaments organized to form sarcomeres, which are joined end-to-end to form myofibrils (see chapter 7). The actin and myosin myofilaments are responsible for muscle contraction, and their organization gives cardiac muscle a striated (banded)

appearance much like that of skeletal muscle. However, the striations are less regularly arranged and less numerous than in skeletal muscle.

Figure 12.13 APR **Cardiac Muscle Cells**

(*a*) Cardiac muscle cells are branching cells with centrally located nuclei. The cells are joined to one another by intercalated disks, which allow action potentials to pass from one cardiac muscle cell to the next. (*b*) In a light micrograph of cardiac muscle tissue, the muscle fibers appear striated because of the arrangement of the individual myofilaments. (*c*) As in skeletal muscle, sarcomeres join end-to-end to form myofibrils, and mitochondria provide ATP for contraction. Sarcoplasmic reticulum and T tubules are visible but are not as numerous as they are in skeletal muscle.

(b) ©Ed Reschke

Like skeletal muscle, cardiac muscle relies on Ca^{2+} and ATP for contraction. Calcium ions enter cardiac muscle cells in response to action potentials and activate the process of contraction much as they do in skeletal muscle. ATP production occurs primarily in mitochondria and depends on O_2 availability. Cardiac muscle cells have many mitochondria, which produce ATP at a rate rapid enough to sustain the normal energy requirements of cardiac muscle. An extensive capillary network provides adequate O_2 to the cardiac muscle cells. Unlike skeletal muscle, cardiac

muscle cannot develop a significant oxygen deficit. Development of a large oxygen deficit could result in muscular fatigue and cessation of cardiac muscle contraction.

Cardiac muscle cells are organized into spiral bundles or sheets (see figure 12.9). When cardiac muscle fibers contract, not only do the muscle fibers shorten but the spiral bundles twist to compress the contents of the heart chambers. Cardiac muscle cells are bound end-to-end and laterally to adjacent cells by specialized cell-to-cell contacts called **intercalated** (in-TER-kah-lay-ted) **disks** (figure 12.13). The membranes of the intercalated disks are highly folded, and the adjacent cells fit together, greatly increasing contact between them and preventing cells from pulling apart. Specialized cell membrane structures in the intercalated disks called **gap junctions** (see chapter 4) allow cytoplasm to flow freely between cells. This enables action potentials to pass quickly and easily from one cell to the next. The cardiac muscle cells of the atria or ventricles, therefore, contract at nearly the same time. The heart's highly coordinated pumping action depends on this characteristic.

12.5 STIMULATION OF THE HEART

Learning Outcomes *After reading this section, you should be able to*

A. Explain the relationship between stimulation of the heart and contraction of cardiac muscle.

B. Describe the characteristics of action potentials in cardiac muscle.

C. Explain the structure and function of the conduction system of the heart.

D. Describe the waves of an electrocardiogram, and relate each of them to contractions of the heart.

Muscle contractions do not occur unless the muscle has been stimulated. In chapter 7 we discussed the relationship between the stimulation of skeletal muscle fibers and the sequence of events that leads to contraction of those same muscle fibers. Similarly, cardiac muscle cells must be stimulated before they contract. Recall from section 12.3 that blood flows from the atria into the ventricles and then out of the heart through the great arteries. The movement of blood through the heart is determined by a coordinated sequence of cardiac muscle contractions, with atrial contraction first, followed by ventricular contraction. Figure 12.14 illustrates the coordination of the stimulation and contraction of the areas of the heart.

❶ The heart is at rest and all chambers are relaxed.

❷ Cardiac muscle cells in the atrial wall are stimulated as action potentials spread across the atrial wall and towards the ventricles.

❸ Cardiac muscle cells in the atrial wall contract, pushing blood into the ventricles.

❹ Cardiac muscle cells in the ventricular wall are stimulated as action potentials spread across the ventricular wall from the apex of the heart towards its base.

❺ Cardiac muscle cells in the ventricular wall contract, pushing blood into the great arteries.

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PROCESS Figure

PROCESS Figure 12.14 Coordination of Cardiac Muscle Stimulation and Contraction.

Cardiac muscle contraction occurs following stimulation by action potentials. The sequence of stimulation ensures that the heart contracts in a coordinated, predictable pattern, with atria contracting first, followed by ventricular contraction.

Understand **During which step of this process is blood flowing through the atrioventricular valves? the semilunar valves?**

Action Potentials in Cardiac Muscle

Like action potentials in skeletal muscle and neurons, those in cardiac muscle exhibit depolarization followed by repolarization. In cardiac muscle, however, a period of slow repolarization greatly prolongs the action potential (figure 12.15). In contrast to action potentials in skeletal muscle, which take less than 2 milliseconds (ms) to complete, action potentials in cardiac muscle take approximately 200 to 500 ms to complete. In addition, unlike in skeletal muscle, in which an action potential is initiated at each cell by a motor neuron (see chapter 7), action potentials in cardiac muscle can spread from one cell to adjacent cells through gap junctions at intercalated disks.

Figure 12.15 Comparison of Action Potentials in Skeletal and Cardiac Muscle

(*a*) An action potential in skeletal muscle consists of depolarization and repolarization phases. The refractory period is indicated by the *purple* shaded area. (*b*) An action potential in cardiac muscle consists of depolarization, plateau, and repolarization phases. Cardiac muscle does not repolarize as rapidly as skeletal muscle (*indicated by the break in the curve*) because of the plateau phase. Due to the prolonged action potential and refractory period (indicated by the *purple* shaded area), cardiac muscle contracts and relaxes almost completely before another action potential can be produced.

In cardiac muscle, each action potential consists of a **depolarization phase** followed by a period of slow repolarization called the **plateau phase.** At the end of the plateau phase, a rapid **repolarization phase** takes place. During the final repolarization phase, the membrane potential achieves its maximum degree of repolarization (figure 12.15*b*) and returns to the resting membrane potential.

The opening and closing of membrane channels are responsible for the changes in the permeability of the cell membrane that produce action potentials (see chapter 8). The initial, rapid depolarization phase of the action potential results from the opening of voltage-gated Na^+ channels, which increases the permeability of the cell membrane to Na^+. Sodium ions then diffuse into the cell, causing depolarization.

The depolarization of cardiac muscle fibers by Na^+ is critical for the next steps in producing contractions of cardiac muscle. Sodium entry triggers opening of voltage-gated Ca^{2+} channels, and Ca^{2+} begins diffusing into the cell, contributing to the overall depolarization. At the peak of depolarization, the Na^+ channels close, and a small number of K^+ channels open. However, the Ca^{2+} channels remain open. Thus, the exit of K^+ from the cell is counteracted by the continued movement of Ca^{2+} into the cell. Consequently, the plateau phase is primarily the result of the opening of voltage-regulated Ca^{2+} channels. The slow diffusion of Ca^{2+} into the cell is the reason the cardiac muscle fiber action potential lasts longer than the action potentials in skeletal muscle fibers. The plateau phase ends, and the repolarization phase begins as the Ca^{2+} channels close and many K^+ channels open, allowing K^+ to move out of the cell.

Action potentials in cardiac muscle exhibit a **refractory period,** like that of action potentials in skeletal muscle and in neurons. The refractory period lasts about as long as the plateau phase of the action potential in cardiac muscle. The prolonged action potential and refractory period allow

cardiac muscle to contract and relax almost completely before another action potential can be produced. Also, the long refractory period in cardiac muscle prevents tetanic, sustained contractions from occurring, thus ensuring a rhythm of contraction and relaxation for cardiac muscle. Therefore, action potentials in cardiac muscle are different from those in skeletal muscle because the plateau phase makes the action potential and its refractory period last longer.

Apply It 2

Why is it important to prevent tetanic contractions in cardiac muscle but not in skeletal muscle?

Conduction System of the Heart

Unlike skeletal muscle that requires neural stimulation to contract, cardiac muscle can contract without neural stimulations. Contraction of the atria and ventricles is coordinated by specialized cardiac muscle cells in the heart wall that form the **conduction system of the heart** (figure 12.16).

PROCESS Figure

PROCESS Figure 12.16 APR Conduction System of the Heart

The conduction system of the heart is composed of specialized cardiac muscle cells that produce spontaneous action potentials. The organization of the conduction system of the heart ensures the proper pattern of contractions of the atria and ventricle, ensuring blood flow.

Why is it important for stimulation of the ventricles to begin at the apex and spread toward the base?

All the cells of the conduction system can produce spontaneous action potentials. The conduction system of the heart includes (1) the sinoatrial node, (2) atrioventricular node, (3) atrioventricular bundle, (4) the bundle branches, and (5) Purkinje fibers. The **sinoatrial (SA) node,** which functions as the heart's pacemaker, is located in the superior wall of the right atrium and initiates the contraction of the heart. The SA node produces action potentials at a faster rate than other areas of the heart and has a larger number of Ca^{2+} channels than other cells in the heart. In addition, the Na^{+} and Ca^{2+} channels in the SA node spontaneously open and close at a rhythmic rate. The heart rate can be affected by certain drugs. Calcium channel blocking agents, for example, are drugs that slow the heart by decreasing the rate of action potential production in the SA node. Calcium channel blockers decrease the rate at which Ca^{2+} moves through Ca^{2+} channels. As a result, it takes longer for depolarization to reach threshold, and the interval between action potentials increases.

Figure 12.16 illustrates the pathways action potentials would follow through the conduction system of the heart.

1. Action potentials originate in the SA node and spread through the myocardium of the right and left atrium, causing atrial contraction.
2. Action potentials reach the **atrioventricular (AV)** (AY-tree-oh-ven-TRIK-you-lar) **node,** located in the lower portion of the right atrium. When action potentials reach the AV node, they spread slowly through it and then into the **atrioventricular (AV) bundle,** a group of specialized cardiac muscle cells in the interventricular septum. The slow rate of action potential conduction in the AV node allows the atria to complete their contraction before action potentials are delivered to the ventricles.

❸ The AV bundle then divides into two branches of conducting tissue, called the **left** and **right bundle branches.** Action potentials pass down the bundle branches toward the apex of the heart.

❹ At the tips of the left and right bundle branches, the conducting tissue forms many small bundles of **Purkinje** (per-KIN-jee) **fibers.** The Purkinje fibers pass to the apex of the heart and then extend to the cardiac muscle of the ventricle walls.

The AV bundle, the bundle branches, and the Purkinje fibers are composed of specialized cardiac muscle fibers that conduct action potentials more rapidly than do other cardiac muscle fibers. Consequently, action potentials are rapidly delivered to all the cardiac muscle of the ventricles. The coordinated contraction of the ventricles depends on the conduction of action potentials by the conduction system. The organization of the conduction system of the heart, particularly the Purkinje fibers, ensures that ventricular contractions begin at the apex and then spread up the ventricular walls. This pattern of movement pushes the blood up toward the great vessels (see figure 12.10).

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Apply It 3

If blood supply is reduced in a small area of the heart through which the left bundle branch passes, how will this affect ventricular contraction?

Following their contraction, the ventricles begin to relax. After the ventricles have completely relaxed, another action potential originates in the SA node to begin the next cycle of contractions.

The SA node is the pacemaker of the heart, but other cells of the conduction system are also capable of producing action potentials spontaneously. For example, if the SA node is unable to function, another area, such as the AV node, becomes the pacemaker. The resulting heart rate is much slower than normal. When action potentials originate in an area of the heart other than the SA node, the result is called an **ectopic** (ek-TOP-ik) **beat.**

Ectopic beats may cause very small portions of the heart to contract rapidly and independently of all other areas. This condition, called **fibrillation** (fih-brih-LAY-shun), reduces the output of the heart to only a

few milliliters of blood per minute when it occurs in the ventricles. Unless ventricular fibrillation is stopped, the person dies in just a few minutes.

To stop the process of fibrillation, health professionals use a technique called defibrillation, in which they apply a strong electrical shock to the chest region. The shock causes simultaneous depolarization of all cardiac muscle fibers. Following depolarization, the SA node can recover and produce action potentials before any other area of the heart. Consequently, the normal pattern of action potential generation and the normal rhythm of contraction are reestablished.

Electrocardiogram

Action potentials conducted through the heart during the cardiac cycle produce electrical currents that can be measured at the surface of the body. Electrodes placed on the body surface and attached to a recording device can detect the small electrical changes resulting from the action potentials in all of the cardiac muscle cells. The record of these electrical events is an **electrocardiogram** (ee-LEK-troh-KAR-dee-oh-gram; **ECG** or **EKG**) (figure 12.17).

Figure 12.17 Electrocardiogram

The major waves and intervals of an electrocardiogram are labeled. Each thin horizontal line on the ECG recording represents 1 millivolt (mV), and each thin vertical line represents 0.04 second.

The normal ECG consists of a (1) P wave, (2) a QRS complex, and (3) a T wave. The **P wave** results from depolarization of the atrial myocardium, and the beginning of the P wave precedes the onset of atrial contraction. The **QRS complex** consists of three individual waves: the Q, R, and S waves. The QRS complex results from depolarization of the ventricles, and the beginning of the QRS complex precedes ventricular contraction. The **T wave** represents repolarization of the ventricles, and the beginning of the T wave precedes ventricular relaxation. A wave representing repolarization of the atria cannot be seen because it occurs during the QRS complex.

The time between the beginning of the P wave and the beginning of the QRS complex is the **PQ interval,** commonly called the **PR interval** because the Q wave is very small. During the PQ interval, the atria contract and begin to relax. At the end of the PQ interval, the ventricles begin to depolarize. The **QT interval** extends from the beginning of the QRS complex to the end of the T wave and represents the length of time required for ventricular depolarization and repolarization.

MICROBES IN YOUR BODY

How Bacteria Affect Cardiac Muscle

You've learned that the majority of bacteria are either harmless or an integral part of our well-being. Unfortunately, there are a handful of pathogenic bacteria that can interfere with the body's homeostasis.

Most people associate bacterial pneumonia with the lungs only. However, in the medical community, it is well known that pneumonia can cause serious heart problems. In fact, cardiac problems cause 70% of the deaths in individuals with other types of severe bacterial infections. Most bacterial pneumonia is caused by the bacterium *Streptococcus pneumoniae*, but until recently the mechanism by which this pathogen damages the heart had not been well understood. It seems that these bacteria induce the cells lining blood vessels to endocytose them and deposit them in cardiac muscle tissue. There, the bacteria release a toxin, called pneumolysin, which kills the cardiac muscle cells. These areas of dead cardiac muscle are called microlesions. In addition, during recovery from the infection, scars may form within

the myocardium. Thus, the bacteria physically damage the heart, which interrupts the electrical signal necessary for cardiac muscle contraction. In addition, simply treating pneumonia with the traditional antibiotic, ampicillin, may actually worsen damage to the heart. Ampicillin causes the bacterial cell walls to burst, which releases a surge of pneumolysin, creating even more microlesions. Use of an antibiotic that does not destroy the bacterial cell walls will help reduce cardiac muscle death. Further, a vaccine against the bacterial molecule that induces the bacterial transport and against pneumolysin has shown great promise in minimizing the tissue damage caused by these bacteria.

Although pathogenic bacteria exist, modern medicine continues to make great strides to reduce their damaging effects on our bodies. In addition, the more we learn about our microbiome, the more effectively we may be able to prevent bacterial infections from occurring in the first place.

Apply It 4

Given that Streptococcus pneumoniae microlesions interrupt the electrical activity that flows between cardiac muscle cells, the heart can experience severe stress and may malfunction or stop contracting altogether. Using what you learned about skeletal muscle contraction, would microlesions in skeletal muscle cause the same type of reaction as in cardiac muscle?

It is important to note that the ECG is a record of electrical events of the heart and is not a direct measurement of mechanical events. This means that neither the force of contraction nor the blood pressure can be determined from an ECG. However, each deflection in the ECG record indicates an electrical event within the heart and correlates with a subsequent mechanical event. Consequently, the ECG is an extremely valuable tool for diagnosing a number of cardiac abnormalities, particularly because it is painless, easy to record, and nonsurgical. Analysis of an ECG can reveal abnormal heart rates or rhythms; problems in conduction pathways, such as blockages; hypertrophy or atrophy of portions of the heart; and the approximate location of damaged cardiac muscle. Table 12.1 describes several conditions associated with abnormal heart rhythms.

TABLE 12.1 Abnormal Heart Rhythms

Condition	Symptoms	Possible Causes

Condition	Symptoms	Possible Causes
Tachycardia	Heart rate in excess of 100 beats per minute (bpm)	Elevated body temperature, excessive sympathetic stimulation, toxic conditions
Bradycardia	Heart rate less than 60 bpm	Increased stroke volume in athletes, excessive vagus nerve stimulation, nonfunctional SA node, carotid sinus syndrome
Sinus arrhythmia	Heart rate varies as much as 5% during respiratory cycle and up to 30% during deep respiration	Cause not always known; occasionally caused by ischemia, inflammation, or cardiac failure
Paroxysmal atrial tachycardia	Sudden increase in heart rate to 150–250 bpm for a few seconds or even for several hours; P waves precede every QRS complex; P wave is inverted and superimposed on T wave	Excessive sympathetic stimulation, abnormally elevated permeability of cardiac muscle to Ca^{2+}
Atrial flutter	As many as 300 P waves/min and 125 QRS complexes/min; resulting in two or three P waves (atrial contractions) for every QRS complex (ventricular contraction)	Ectopic beats in atria
Atrial fibrillation	No P waves, normal QRS and T waves, irregular timing; ventricles are constantly stimulated by atria; reduced ventricle filling; increased chance of fibrillation	Ectopic beats in atria
Ventricular tachycardia	Frequently causes fibrillation	Often associated with damage to AV node or ventricular muscle

Apply It 5

Explain how the ECGs would appear for a person who has a damaged left bundle branch (see Apply It 3) and for a person who has many ectopic beats originating from her atria.

12.6 CARDIAC CYCLE

Learning Outcome *After reading this section, you should be able to*

A. Describe the cardiac cycle and the relationships among the contraction of each of the chambers, the pressure in each of the chambers, the phases of the electrocardiogram, and the heart sounds.

The right and left halves of the heart can be viewed as two separate pumps. Each pump consists of a primer pump—the atrium—and a power pump—the ventricle. The atria act as primer pumps because they complete the filling of the ventricles with blood, and the ventricles act as power pumps because they produce the major force that causes blood to flow through the pulmonary and systemic circulations. The term **cardiac cycle** refers to the repetitive pumping process that begins with the onset of cardiac muscle contraction and ends with the beginning of the next contraction (figure 12.18). Pressure changes produced within the heart chambers as a result of cardiac muscle contraction move blood from areas of higher pressure to areas of lower pressure.

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PROCESS Figure

PROCESS Figure 12.18 APR Cardiac Cycle

The cardiac cycle is the sequence of events that occurs from the beginning of one heartbeat to the beginning of the next heartbeat, during which time the atria and ventricles contract, ensuring blood flow.

Understand Often, ventricular systole is divided into two phases: the isovolumetric (same-volume) phase and the ventricular ejection phase. What are some differences between these two phases?

Atrial systole (SIS-toh-lee; a contracting) refers to contraction of the two atria. **Ventricular systole** refers to contraction of the two ventricles. **Atrial diastole** (die-AS-toh-lee; dilation) refers to relaxation of the two atria, and **ventricular diastole** refers to relaxation of the two ventricles. When the terms *systole* and *diastole* are used alone, they refer to ventricular contraction or relaxation. The ventricles contain more cardiac muscle than the atria and produce far greater pressures, which force blood to circulate throughout the vessels of the body.

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During the cardiac cycle, changes in chamber pressure and the opening and closing of the heart valves determine the direction of blood movement. As the cardiac cycle is described, it is important to focus on these pressure changes and heart valve movements. Before we start, it is also important to have a clear image of the state of the heart. At the beginning of the cardiac cycle, the atria and ventricles are relaxed, the AV valves are open, and the semilunar valves are closed. Figure 12.18 illustrates the major events of the cardiac cycle.

❶ Blood returning to the heart first enters the atria. Since the AV valves are open, blood flows into the ventricles, filling them to approximately 70% of their volume.

❷ *Atrial systole*—The atria contract, forcing additional blood to flow into the ventricles to complete their filling. The semilunar valves remain closed.

❸ *Ventricular systole*—At the beginning of ventricular systole, contraction of the ventricles pushes blood toward the atria, causing the AV valves to close as the pressure in the ventricles begins to increase.

❹ As ventricular systole continues, the increasing pressure in the ventricles exceeds the pressure in the pulmonary trunk and aorta, the semilunar valves are forced open, and blood is ejected into the pulmonary trunk and aorta.

❺ *Ventricular diastole*—At the beginning of ventricular diastole, the pressure in the ventricles decreases below the pressure in the aorta and pulmonary trunk. The semilunar valves close and prevent blood from flowing back into the ventricles. As diastole continues, the pressure continues to decline in the ventricles until atrial pressures are greater than ventricular pressures. Then the AV valves open, and blood flows directly from the atria into the relaxed ventricles.

During the previous ventricular systole, the atria were relaxed and blood collected in them. When the ventricles relax and the AV valves open, blood flows into the ventricles (see figure 12.18, step 1) and they begin to fill again.

Figure 12.19 displays the main events of the cardiac cycle and should be examined from top to bottom for each period.

1. The ECG indicates the electrical events that cause the atria and ventricles to contract and relax.
2. The pressure graph shows the pressure changes within the left atrium (blue dashed line), left ventricle (black line), and aorta (red dashed line) resulting from atrial and ventricular contraction and relaxation. The pressure changes in the right side of the heart are not shown here, but they are similar to those in the left side, only lower.
3. The volume graph presents the changes in left ventricular volume as blood flows into and out of the left ventricle as a result of the pressure changes.
4. The sound graph records the closing of valves caused by blood flow.

Figure 12.19 **Events of the Cardiac Cycle**

(*Top*) The cardiac cycle is divided into five periods. *From top to bottom,* these graphs show an electrocardiogram; pressure changes for the left atrium (*blue dashed line*), the left ventricle (*black line*), and

the aorta (*red dotted line*); left ventricular volume curve; and the sequence of the heart sounds.

By reviewing the events of each period, you can see that as the atria are stimulated (P wave in Panel 1), we can see an increase in left atrial pressure (blue dashed line in Panel 2). See figure 12.18 for illustrations of the valves and blood flow.

Apply It 6

Describe the effect of a leaky (incompetent) aortic semilunar valve on the volume of blood in the left ventricle just before ventricular contraction. Describe the effect of a severely narrowed opening through the aortic semilunar valves on the amount of work the heart must do to pump the normal volume of blood into the aorta during each beat of the heart.

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12.7 HEART SOUNDS

Learning Outcome ***After reading this section, you should be able to***

A. Describe the heart sounds and their significance.

The **stethoscope** (STETH-oh-skope; *stetho,* the chest) was originally developed to listen to the sounds of the lungs and heart and is now used to listen to other sounds of the body as well. Figure 12.20 shows the sites on the thorax where the heart sounds can best be heard with a stethoscope. There are two main heart sounds. The first heart sound can be represented by the syllable *lubb,* and the second heart sound can be represented by *dupp*. The first heart sound has a lower pitch than the second. The first heart sound occurs at the beginning of ventricular systole and results from closure of the AV valves (see figure 12.18, step 3, and figure 12.19). The second heart sound occurs at the beginning of ventricular diastole and results from closure of the semilunar valves (see figure 12.18, step 5, and figure 12.19). The valves usually do not make sounds when they open.

Figure 12.20 **Location of the Heart Valves in the Thorax**

Surface markings of the heart in an adult male. The positions of the four heart valves are indicated by *blue ellipses,* and the sites where the sounds of the valves are best heard with a stethoscope are indicated by *pink circles.*

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Clinically, ventricular systole occurs between the first and second heart sounds. Ventricular diastole occurs between the second heart sound and the first heart sound of the next beat. Because ventricular diastole lasts longer than ventricular systole, there is less time between the first and second heart sounds than between the second heart sound and the first heart sound of the next beat.

Analyze

Apply It 7

Compare the rate of blood flow out of the ventricles between the first and second heart sounds of the same beat to the rate of blood flow out of the ventricles between the second heart sound of one beat and the first heart sound of the next beat.

In some individuals, a heart valve does not close completely and thus is called an **incompetent valve.** Such valves leak when they are supposed to be closed and allow blood to flow in the reverse direction. For example, an incompetent bicuspid valve allows blood to flow from the left ventricle to

the left atrium during ventricular systole. This reduces the amount of blood pumped into the aorta. It also dramatically increases the blood pressure in the left atrium and in the pulmonary veins during ventricular systole. During diastole, the excess blood pumped into the atrium once again flows into the ventricle, along with the blood that normally flows from the lungs to the left atrium. Therefore, the volume of blood entering the left ventricle is greater than normal. The increased filling of the left ventricle gradually causes it to hypertrophy and can lead to heart failure. The increased pressure in the pulmonary veins can cause edema in the lungs. This information may be useful in answering the Learn to Apply It question at the beginning of the chapter.

Abnormal heart sounds called **murmurs** are usually a result of faulty valves. For example, an incompetent valve fails to close tightly, so blood leaks through the valve when it is closed, making a swishing sound immediately after the valve closes. For example, an incompetent AV valve produces a swishing sound immediately after the first heart sound.

When the opening of a valve is narrowed, or **stenosed** (STEN-ohzd; a narrowing), a swishing sound precedes closure of the stenosed valve. For example, when the bicuspid valve is stenosed, a swishing sound precedes the first heart sound.

Apply It 8

If normal heart sounds are represented by lubb-dupp, lubb-dupp, what does a heart sound represented by lubb-duppshhh, lubb-duppshhh represent? What does lubb-shhhdupp, lubb-shhhdupp represent (assuming that shhh represents a swishing sound)?

12.8 REGULATION OF HEART FUNCTION

Learning Outcomes *After reading this section, you should be able to*

A. Describe intrinsic regulation of the heart.
B. Describe extrinsic regulation of the heart.

Various measurements can be taken to assess the heart's function. **Cardiac output (CO)** is the volume of blood pumped by either ventricle of the heart each minute. **Stroke volume (SV)** is the volume of blood pumped per ventricle each time the heart contracts, and the **heart rate (HR)** is the number of times the heart contracts each minute. Cardiac

output can be calculated by multiplying the stroke volume times the heart rate:

$$\underset{(\text{mL/ min})}{\text{CO}} = \underset{(\text{mL/beat})}{\text{SV}} \times \underset{(\text{beats/ min})}{\text{HR}}$$

Under resting conditions, the heart rate is approximately 72 beats/min, and the stroke volume is approximately 70 mL/beat. Consequently, the cardiac output is slightly more than 5 L/min:

$$\begin{aligned}\text{CO} &= \text{SV} \times \text{HR} \\ &= 70\ \text{mL/beat} \times 72\ \text{bpm} \\ &= 5040\ \text{mL/min (approximately 5 L/min)}\end{aligned}$$

The heart rate and the stroke volume vary considerably among people. Athletes tend to have a higher stroke volume and lower heart rate at rest because exercise has increased the size of their hearts. Nonathletes are more likely to have a higher heart rate and lower stroke volume. During exercise, the heart rate in a nonathlete can increase to 190 bpm, and the stroke volume can increase to 115 mL/beat. Therefore, the cardiac output increases to approximately 22 L/min:

$$\begin{aligned}\text{CO} &= \text{SV} \times \text{HR} \\ &= 115\ \text{mL/beat} \times 190\ \text{bpm} \\ &= 21,850\ \text{mL/min (approximately 22 L/min)}\end{aligned}$$

This cardiac output is several times greater than the cardiac output under resting conditions. Athletes can increase their cardiac output to a greater degree than nonathletes. The control mechanisms that modify the stroke volume and the heart rate are classified as intrinsic and extrinsic.

Intrinsic regulation results from the heart's normal functional characteristics and does not depend on either neural or hormonal regulation. It is functional whether the heart is in place in the body or is removed and maintained outside the body under proper conditions. Extrinsic regulation involves neural and hormonal control. Neural regulation of the heart results from sympathetic and parasympathetic reflexes, and the major hormonal regulation comes from epinephrine and norepinephrine secreted by the adrenal medulla.

Intrinsic Regulation of the Heart

Intrinsic regulation refers to mechanisms contained within the heart itself. An example involves the affect cardiac muscle length has on force of contraction. The force of contraction produced by cardiac muscle is related to the degree of stretch of cardiac muscle fibers. And the degree of stretch of cardiac muscle in the ventricles at the end of ventricular diastole is determined by the amount of blood in the ventricles. You can relate this to filling a balloon with water. As more water (greater volume) is added to the balloon, the wall of the balloon stretches more. **Preload** is the degree to which the ventricular walls are stretched at the end of diastole, and **venous return** is the amount of blood that returns to the heart. If venous return increases, the heart fills to a greater volume and stretches the cardiac muscle fibers, producing a greater preload. In response, cardiac muscle fibers contract with more force. The stronger force of contraction causes an increased volume of blood to be ejected from the heart, resulting in a greater stroke volume. As venous return increases, resulting in a greater preload, cardiac output increases. Conversely, if venous return decreases, resulting in a lower preload, the cardiac output decreases. The relationship between preload and stroke volume is called **Starling's law of the heart.**

Because venous return is influenced by many conditions, Starling's law of the heart has a major influence on cardiac output. For example, muscular activity during exercise causes increased venous return, resulting in increased preload, stroke volume, and cardiac output. This is beneficial because increased cardiac output is needed during exercise to supply O_2 to exercising skeletal muscles.

Afterload refers to the pressure against which the ventricles must pump blood. People suffering from hypertension have an increased afterload because their aortic pressure is elevated during contraction of the ventricles. Recall that left-ventricular pressure must increase above aortic pressure to force open the aortic semilunar valve. The heart must do more work to pump blood from the left ventricle into the aorta, which increases the workload on the heart and can eventually lead to heart failure. A reduced afterload decreases the work the heart must do. People who have lower blood pressure have a reduced afterload and develop heart failure less often than people who have hypertension. However, the afterload influences cardiac output less than preload influences it. The afterload

must increase substantially before it decreases the volume of blood pumped by a healthy heart.

CLINICAL IMPACT

Consequences of Heart Failure

Although heart failure can occur in young people, it usually results from progressive weakening of the heart muscle in elderly people. In heart failure, the heart is not capable of pumping all the blood that is returned to it because further stretching of the cardiac muscle fibers does not increase the stroke volume. Consequently, blood backs up in the veins. For example, heart failure that affects the right ventricle, called **right heart failure,** causes blood to back up in the veins that return blood from systemic vessels to the heart. Filling of the veins with blood causes edema, especially in the legs and feet, due to the accumulation of fluid in the tissues outside blood vessels. Heart failure that affects the left ventricle, called **left heart failure,** causes blood to back up in the veins that return blood from the lungs to the heart. Filling of these veins causes edema in the lungs, which makes breathing difficult.

Extrinsic Regulation of the Heart

Extrinsic regulation includes nervous regulation and chemical regulation.

Nervous Regulation: Baroreceptor Reflex

The autonomic nervous system influences the pumping action of the heart and thereby affects cardiac output by altering both heart rate and stroke volume. Sympathetic and parasympathetic nerve fibers innervate the heart and have a major effect on the SA node. Stimulation by sympathetic nerve fibers causes the heart rate and the stroke volume to increase, whereas stimulation by parasympathetic nerve fibers causes the heart rate to decrease.

The **baroreceptor** (bar-oh-ree-SEP-ter; *baro,* pressure) **reflex** is a mechanism of the nervous system that plays an important role in regulating heart function. **Baroreceptors** are stretch receptors that

monitor blood pressure in the aorta and in the wall of the internal carotid arteries, which carry blood to the brain. Changes in blood pressure result in changes in the stretch of the walls of these blood vessels—and changes in the frequency of action potentials produced by the baroreceptors. The action potentials are transmitted along nerve fibers from the stretch receptors to the medulla oblongata of the brain.

Within the medulla oblongata is a **cardioregulatory center,** which receives and integrates action potentials from the baroreceptors. The cardioregulatory center controls the action potential frequency in sympathetic and parasympathetic nerve fibers that extend from the brain and spinal cord to the heart. The cardioregulatory center also influences sympathetic stimulation of the adrenal gland. Epinephrine and norepinephrine, released from the adrenal gland, increase the stroke volume and heart rate.

Figure 12.21 shows how the baroreceptor reflex keeps the heart rate and stroke volume within normal ranges. When the blood pressure increases, the baroreceptors are stimulated. Action potentials are sent along the nerve fibers to the medulla oblongata at increased frequency. This prompts the cardioregulatory center to increase parasympathetic stimulation and decrease sympathetic stimulation of the heart. As a result, the heart rate and stroke volume decrease, causing blood pressure to decline.

Homeostasis Figure 12.21 APR **Baroreceptor Reflex**

The baroreceptor reflex maintains homeostasis in response to changes in blood pressure. (1) Blood pressure is within its normal range. (2) Blood pressure increases outside the normal range, which causes homeostasis to be disturbed. (3) Baroreceptors in the carotid arteries and aorta detect the increase in blood pressure and the cardioregulatory center in the brain alters autonomic stimulation of the heart. (4) Heart rate and stroke volume

decrease. (5) These changes cause blood pressure to decrease. (6) Blood pressure returns to its normal range, and homeostasis is restored.

When the blood pressure decreases, less stimulation of the baroreceptors occurs. A lower frequency of action potentials is sent to the medulla oblongata of the brain, and this triggers a response in the cardioregulatory center. The cardioregulatory center responds by increasing sympathetic stimulation of the heart and decreasing parasympathetic stimulation. Consequently, the heart rate and stroke volume increase, causing blood pressure to increase. If the decrease in blood pressure is large, sympathetic stimulation of the adrenal medulla also increases. The epinephrine and norepinephrine secreted by the adrenal medulla also increase the heart rate and stroke volume, also causing the blood pressure to increase toward its normal value (figure 12.21).

Apply It 9

In response to a severe hemorrhage, blood pressure lowers, the heart rate increases dramatically, and the stroke volume lowers. If low blood pressure activates a reflex that increases sympathetic stimulation of the heart, why is the stroke volume low?

Chemical Regulation: Chemoreceptor Reflex

Epinephrine and small amounts of norepinephrine released from the adrenal medulla in response to exercise, emotional excitement, or stress also influence the heart's function. Epinephrine and norepinephrine bind to receptor proteins on cardiac muscle and cause increased heart rate and stroke volume. Excitement, anxiety, or anger can affect the cardioregulatory center, resulting in increased sympathetic stimulation of the heart and increased cardiac output. Depression, on the other hand, can increase parasympathetic stimulation of the heart, causing a slight reduction in cardiac output.

The medulla oblongata of the brain also contains chemoreceptors that are sensitive to changes in pH and CO_2 levels. A decrease in pH, often caused by an increase in CO_2, results in sympathetic stimulation of the heart (figure 12.22).

Homeostasis Figure 12.22 APR **Chemoreceptor Reflex—pH**

The chemoreceptor reflex maintains homeostasis in response to changes in blood concentrations of CO2 and H^+ (or pH). (1) Blood pH is within its normal range. (2) Blood pH increases outside the normal range. (3) Chemoreceptors in the medulla oblongata detect increased blood pH. Control centers in the brain decrease sympathetic stimulation of the heart and adrenal medulla. (4) Heart rate and stroke volume decrease, reducing blood flow to lungs. (5) These changes cause blood pH to decrease (as a result of increase in blood CO_2). (6) Blood pH returns to its normal range, and homeostasis is restored.

Changes in the extracellular concentration of K^+, Ca^{2+}, and Na^+, which influence other electrically excitable tissues, also affect cardiac muscle function. An excess of extracellular K^+ causes the heart rate and stroke volume to decrease. If the extracellular K^+ concentration increases further, normal conduction of action potentials through cardiac muscle is blocked, and death can result. An excess of extracellular Ca^{2+} causes the heart to contract arrhythmically. Reduced extracellular Ca^{2+} causes both the heart rate and stroke volume to decrease.

Figure 12.23 summarizes how nervous and chemical factors interact to regulate the heart rate and stroke volume.

PROCESS Figure

PROCESS Figure 12.23 **Summary of Extrinsic Regulation**

Sensory nerves (*green*) carry action potentials from sensory receptors to the medulla oblongata. Sympathetic nerves (*blue*) and parasympathetic nerves (*red*) exit the spinal cord or medulla oblongata and extend to the heart to

regulate its function. Epinephrine and norepinephrine from the adrenal gland also help regulate the heart's action. (SA = sinoatrial)

Cardiac muscle is described as being under involuntary control. Why is it that some individuals can seemingly "control" their heart rate through meditation?

1. Sensory neurons carry action potentials from baroreceptors to the cardioregulatory center. Chemoreceptors in the medulla oblongata influence the cardioregulatory center.
2. The cardioregulatory center controls the frequency of action potentials in the parasympathetic neurons extending to the heart. The parasympathetic neurons decrease the heart rate.
3. The cardioregulatory center controls the frequency of action potentials in the sympathetic neurons extending to the heart. The sympathetic neurons increase the heart rate and the stroke volume.
4. The cardioregulatory center influences the frequency of action potentials in the sympathetic neurons extending to the adrenal medulla. The sympathetic neurons increase the secretion of epinephrine and some norepinephrine into the general circulation. Epinephrine and norepinephrine increase the heart rate and stroke volume.

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SYSTEMS PATHOLOGY

Myocardial Infarction

Paul, an overweight, out-of-shape executive, was a smoker and indulged in high-fat foods. One day at work, Paul felt intense pain in his chest that radiated down his left arm. Out of breath and dizzy, Paul had to lie down on the floor. He became anxious and disoriented and eventually lost consciousness, but he did not stop breathing. Paul's co-worker noticed him and called 911. Paramedics arrived and found that Paul's blood pressure was low and he exhibited arrhythmia and tachycardia. They conducted an ECG and administered O_2 and medication to control the arrhythmia.

At the hospital, Paul was given tissue plasminogen activator (t-PA) to improve blood flow to the damaged area of the heart. Paul remained in the hospital. Over the next few days, blood levels of enzymes, such as creatine phosphokinase, increased in Paul's blood, which confirmed that cardiac muscle had been damaged by an

infarction. Paul also began to experience shortness of breath because of pulmonary edema, and after a few days he developed pneumonia. He was treated for the pneumonia, and his condition gradually improved over the next few weeks. An **angiogram** (AN-jee-oh-gram; *angeion*, a vessel + *gramma*, a writing) (figure 12.24), which is an imaging technique used to visualize the coronary arteries, was performed several days after Paul's infarction. The angiogram showed some restricted blood flow in Paul's coronary arteries and a permanent reduction in a significant part of the lateral wall of Paul's left ventricle, but his physicians decided neither angioplasty nor bypass surgery was necessary.

Figure 12.24 Angiogram

An angiogram is a picture of a blood vessel that is usually obtained by injecting the blood vessel with dye that can be detected by x-rays. Note the partially occluded (blocked) coronary blood vessel in this angiogram on the left, which has been computer-enhanced to show colors. The angiogram on the right is of a normal heart.

(*left*) CNRI/Science Source (*right*) ©SPL/Science Source

Apply It 10

Severe ischemia in the wall of a ventricle can cause the death of cardiac muscle cells. Inflammation develops around the necrotic (dead) tissue, and macrophages invade and phagocytize dead cells. At the same time, blood vessels and connective tissue grow into the necrotic area and begin to deposit connective tissue to replace the necrotic tissue. While Paul was still recovering in the hospital, another patient was admitted with a similar condition. After about a week, that person's blood pressure suddenly decreased to very low levels, and he died within a short time. An autopsy revealed a large amount of blood in

the pericardial sac and a rupture in the wall of the left ventricle. Explain these effects.

Paul experienced a myocardial infarction in which a thrombosis in one of the branches of the left coronary artery reduced blood supply to the lateral wall of the left ventricle, resulting in ischemia of the left ventricle wall (figure 12.24). The fact that t-PA, which activates plasminogen and thereby dissolves blood clots, was an effective treatment supports the conclusion that the infarction was due to a thrombosis. An ischemic area of the heart wall was not able to contract normally; therefore, the heart's pumping effectiveness was dramatically reduced. The reduced pumping capacity was responsible for the low blood pressure, which decreased the blood flow to Paul's brain, resulting in confusion, disorientation, and unconsciousness.

Low blood pressure, increasing blood CO_2 levels, pain, and anxiousness increased sympathetic stimulation of the heart and adrenal glands. Increased sympathetic stimulation of the adrenal medulla caused the release of epinephrine. Increased parasympathetic stimulation of the heart resulted from pain sensations. The heart rate was periodically arrhythmic due to the combined effects of parasympathetic stimulation, sympathetic stimulation, and the release of epinephrine and norepinephrine from the adrenal gland. In addition, the ischemic areas of the left ventricle produced ectopic beats.

Myocardial infarctions can lead to dysfunction in other systems of the body (figure 12.25). In Paul's case, pulmonary edema resulted from the increased pressure in the pulmonary veins because of the left ventricle's reduced ability to pump blood. The edema allowed bacteria to infect the lungs and cause pneumonia.

Figure 12.25 Systems Interactions: Myocardial Infarction

A myocardial infarction can affect many systems of the body, as this diagram illustrates.

The heart began to beat rhythmically in response to medication because the infarction had not damaged the heart's conducting system, which is an indication that there were no permanent arrhythmias. (Permanent arrhythmias are indications of damage done to cardiac muscle cells specialized to conduct action potentials in the heart.)

Paul's physician recommended a weight-loss program and a low-sodium and low-fat diet. He also advised Paul to take a small amount of aspirin regularly and to stop smoking. He explained that Paul would have to take medication for high blood pressure if his blood pressure did not decrease in response to the recommended changes. The physician recommended an aerobic exercise program after a period of recovery and suggested that Paul seek ways to reduce the stress associated with his job. Paul followed the doctor's recommendations, and after several months, his blood pressure was normal, and he felt better than he had in years.

TABLE 12.2	REPRESENTATIVE DISEASES AND DISORDERS: Heart
Condition	**Description**
Inflammation of Heart Tissue	

Condition	Description
Endocarditis	Inflammation of the endocardium; affects the valves more severely than other areas of the endocardium; may lead to scarring, causing stenosed or incompetent valves
Cardiomyopathy	Disease of the myocardium of unknown cause or occurring secondarily to other disease; results in weakened cardiac muscle, causing all chambers of the heart to enlarge; may eventually lead to congestive heart failure
Rheumatic heart disease	Results from a streptococcal infection in young people; toxin produced by the bacteria can cause rheumatic fever several weeks after the infection that can result in rheumatic endocarditis
Reduced Blood Flow to Cardiac Muscle	
Coronary heart disease	Reduces the amount of blood the coronary arteries can deliver to the myocardium; see Clinical Impact, "Heart Attack"
Coronary thrombosis	Formation of blood clot in a coronary artery
Congenital Heart Diseases (Occur at Birth)	
Septal defect	Hole in the septum between the left and right sides of the heart, allowing blood to flow from one side of the heart to the other and greatly reducing the heart's pumping effectiveness
Patent ductus arteriosus	Ductus arteriosus fails to close after birth, allowing blood to flow from the aorta to the pulmonary trunk under a higher pressure, which damages the lungs; also, the left ventricle must work harder to maintain adequate systemic pressure

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Body temperature affects the metabolism in the heart just as it affects other tissues. Elevated body temperature increases the heart rate, and reduced body temperature slows the heart rate. For example, the heart rate is usually elevated when a person has a fever. During heart surgery, the body temperature is sometimes intentionally lowered to slow the heart rate and metabolism.

EFFECTS OF AGING ON THE HEART

Gradual changes in heart function are associated with aging. These changes are minor under resting conditions but become more obvious during exercise and in response to age-related diseases.

By age 70, a person's cardiac output has probably decreased by approximately one-third. Because of the decrease in the reserve strength of the heart, many elderly people have a limited ability to respond to emergencies, infections, blood loss, or stress.

Hypertrophy (enlargement) of the left ventricle is a common age-related change. This appears to result from a gradual increase in the pressure in the aorta (afterload), against which the left ventricle must pump. The increased aortic pressure results from a gradual decrease in the aorta's elasticity. Because the left ventricle is enlarged, its ability to pump out blood is reduced, which can cause an increase in left atrial pressure and lead to increased pulmonary edema. Consequently, older people tend to feel out of breath when they exercise strenuously.

Aging cardiac muscle requires a greater amount of time to contract and relax. Thus, the maximum heart rate decreases. Both the resting and maximum cardiac output slowly lower as people grow older, and by age 85, the cardiac output has decreased 30–60%.

Age-related changes also affect the connective tissue of the heart valves. The connective tissue becomes less flexible, and calcium deposits develop in the valves. As a result, the aortic semilunar valve may become stenosed or incompetent.

An age-related increase in cardiac arrhythmias occurs as a consequence of a decreased number of cardiac cells in the SA node and because of cell replacement in the AV bundle.

Coronary artery disease and heart failure are also age-related. Approximately 10% of elderly people over age 80 have heart failure, and a major contributing factor is coronary heart disease. Advanced age, malnutrition, chronic infections, toxins, severe anemias, hyperthyroidism, and hereditary factors can also lead to heart failure.

Exercise has many beneficial effects on the heart. Regular aerobic exercise improves the heart's functional capacity at all ages, providing the person has no other conditions that cause the increased workload on the heart to be harmful.

SUMMARY

12.1 Functions of the Heart

1. The heart generates blood pressure.
2. The heart routes blood through the systemic and pulmonary circulations.
3. The heart's pumping action and its valves ensure a one-way flow of blood through the heart and blood vessels.
4. The heart helps regulate blood supply to tissues.

12.2 Size, Form, and Location of the Heart

The heart is approximately the size of a closed fist and is located in the pericardial cavity.

12.3 Anatomy of the Heart

Pericardium

1. The pericardium is a sac consisting of fibrous and serous pericardia. The fibrous pericardium is lined by the parietal pericardium.
2. The outer surface of the heart is lined by the visceral pericardium (epicardium).
3. Between the visceral and parietal pericardia is the pericardial cavity, which is filled with pericardial fluid.

External Anatomy

1. The atria are separated externally from the ventricles by the coronary sulcus. The right and left ventricles are separated externally by the interventricular sulci.
2. The inferior and superior venae cavae enter the right atrium. The four pulmonary veins enter the left atrium.
3. The pulmonary trunk exits the right ventricle, and the aorta exits the left ventricle.

Heart Chambers and Internal Anatomy

1. There are four chambers in the heart. The left and right atria receive blood from veins and function mainly as reservoirs. Contraction of the atria

completes ventricular filling.

2. The atria are separated internally from each other by the interatrial septum.
3. The ventricles are the main pumping chambers of the heart. The right ventricle pumps blood into the pulmonary trunk, and the left ventricle, which has a thicker wall, pumps blood into the aorta.
4. The ventricles are separated internally by the interventricular septum.

Heart Valves

1. The heart valves ensure one-way flow of blood.
2. The tricuspid valve (three cusps) separates the right atrium and the right ventricle, and the bicuspid valve (two cusps) separates the left atrium and the left ventricle.
3. The papillary muscles attach by the chordae tendineae to the cusps of the tricuspid and bicuspid valves and adjust tension on the valves.
4. The aorta and pulmonary trunk are separated from the ventricles by the semilunar valves.
5. The skeleton of the heart is a plate of fibrous connective tissue that separates the atria from the ventricles, acts as an electrical barrier between the atria and ventricles, and supports the heart valves.

Route of Blood Flow Through the Heart

1. The left and right sides of the heart can be considered separate pumps.
2. Blood flows from the systemic vessels to the right atrium and from the right atrium to the right ventricle. From the right ventricle, blood flows to the pulmonary trunk and from the pulmonary trunk to the lungs. From the lungs, blood flows through the pulmonary veins to the left atrium, and from the left atrium, blood flows to the left ventricle. From the left ventricle, blood flows into the aorta and then through the systemic vessels.

Blood Supply to the Heart

1. The left and right coronary arteries originate from the base of the aorta and supply the heart.
2. The left coronary artery has three major branches: the anterior interventricular, the circumflex, and the left marginal arteries.

3. The right coronary artery has two major branches: the posterior interventricular and the right marginal arteries.
4. Blood returns from heart tissue through cardiac veins to the coronary sinus and into the right atrium. Small cardiac veins also return blood directly to the right atrium.

12.4 Histology of the Heart

Heart Wall

The heart wall consists of the outer epicardium, the middle myocardium, and the inner endocardium.

Cardiac Muscle

1. Cardiac muscle is striated; it depends on ATP for energy and on aerobic metabolism.
2. Cardiac muscle cells are joined by intercalated disks that allow action potentials to be propagated throughout the heart.

12.5 Stimulation of the Heart

The movement of blood through the heart is determined by a coordinated sequence of cardiac muscle contractions: atria contract first, followed by ventricular contraction.

Action Potentials in Cardiac Muscle

1. Action potentials in cardiac muscle are prolonged compared to those in skeletal muscle and have a depolarization phase, a plateau phase, and a repolarization phase.
2. The depolarization is due mainly to opening of the voltage-gated Na^+ channels, and the plateau phase is due to opened voltage-gated Ca^{2+} channels. Repolarization at the end of the plateau phase is due to the opening of K^+ channels for a brief period.
3. The prolonged action potential in cardiac muscle ensures that contraction and relaxation occur and prevents tetany.
4. The SA node located in the upper wall of the right atrium is the normal pacemaker of the heart, and cells of the SA node have more voltage-gated Ca^{2+} channels than do other areas of the heart.

Conduction System of the Heart

1. The conduction system of the heart is made up of specialized cardiac muscle cells.
2. The SA node produces action potentials that are propagated over the atria to the AV node.
3. The AV node and the atrioventricular bundle conduct action potentials to the ventricles.
4. The right and left bundle branches conduct action potentials from the atrioventricular bundle through Purkinje fibers to the ventricular muscle.
5. An ectopic beat results from an action potential that originates in an area of the heart other than the SA node.

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Electrocardiogram

1. An ECG is a record of electrical events within the heart.
2. An ECG can be used to detect abnormal heart rates or rhythms, abnormal conduction pathways, hypertrophy or atrophy of the heart, and the approximate location of damaged cardiac muscle.
3. A normal ECG consists of a P wave (atrial depolarization), a QRS complex (ventricular depolarization), and a T wave (ventricular repolarization).
4. Atrial contraction occurs during the PQ interval, and the ventricles contract and relax during the QT interval.

12.6 Cardiac Cycle

1. Atrial systole is contraction of the atria, and ventricular systole is contraction of the ventricles. Atrial diastole is relaxation of the atria, and ventricular diastole is relaxation of the ventricles.
2. During atrial systole, the atria contract and complete filling of the ventricles.
3. During ventricular systole, the AV valves close, pressure increases in the ventricles, the semilunar valves are forced open, and blood flows into the

aorta and pulmonary trunk.

4. At the beginning of ventricular diastole, pressure in the ventricles decreases. The semilunar valves close to prevent backflow of blood from the aorta and pulmonary trunk into the ventricles.
5. When the pressure in the ventricles is low enough, the AV valves open, and blood flows from the atria into the ventricles.

12.7 Heart Sounds

1. The first heart sound results from closure of the AV valves. The second heart sound results from closure of the semilunar valves.
2. Abnormal heart sounds, called murmurs, can result from incompetent (leaky) valves or stenosed (narrowed) valves.

12.8 Regulation of Heart Function

Cardiac output (volume of blood pumped per ventricle per minute) is equal to the stroke volume (volume of blood ejected per beat) times the heart rate (beats per minute).

Intrinsic Regulation of the Heart

1. *Intrinsic regulation* refers to regulation mechanisms contained within the heart.
2. As venous return to the heart increases, the heart wall is stretched, and the increased stretch of the ventricular walls is called preload.
3. A greater preload causes the cardiac output to increase because stroke volume increases (Starling's law of the heart).
4. Afterload is the pressure against which the ventricles must pump blood.

Extrinsic Regulation of the Heart

1. *Extrinsic regulation* refers to nervous and chemical mechanisms.
2. Sympathetic stimulation increases stroke volume and heart rate; parasympathetic stimulation decreases heart rate.
3. The baroreceptor reflex detects changes in blood pressure. If blood pressure increases suddenly, the reflex causes a decrease in heart rate and stroke

volume; if blood pressure decreases suddenly, the reflex causes an increase in heart rate and stroke volume.

4. Emotions influence heart function by increasing sympathetic stimulation of the heart in response to exercise, excitement, anxiety, or anger and by increasing parasympathetic stimulation in response to depression.
5. Alterations in body fluid levels of CO_2, pH, and ion concentrations, as well as changes in body temperature, influence heart function.

REMEMBERING AND UNDERSTANDING

1. Describe the size and location of the heart, including its base and apex.
2. Describe the structure and function of the pericardium.
3. What chambers make up the left and right sides of the heart? What are their functions?
4. Describe the structure and location of the tricuspid, bicuspid, and semilunar valves. What is the function of these valves?
5. What are the functions of the atria and ventricles?
6. Starting in the right atrium, describe the flow of blood through the heart.
7. Describe the vessels that supply blood to the cardiac muscle.
8. Define heart attack and infarct. How does atherosclerotic plaque affect the heart?
9. Describe the three layers of the heart. Which of the three layers is most important in causing contractions of the heart?
10. Describe the structure of cardiac muscle cells, including the structure and function of intercalated disks.

11. Describe the events that result in an action potential in cardiac muscle.
12. Explain how cardiac muscle cells in the SA node produce action potentials spontaneously and why the SA node is the heart's pacemaker.
13. What is the function of the conduction system of the heart? Starting with the SA node, describe the route of an action potential as it goes through the conduction system of the heart.
14. Explain the electrical events that generate each portion of the electrocardiogram. How do they relate to contraction events?
15. What contraction and relaxation events occur during the PQ interval and the QT interval of the electrocardiogram?
16. Define cardiac cycle, systole, and diastole.
17. Describe blood flow and the opening and closing of heart valves during the cardiac cycle.
18. Describe the pressure changes that occur in the left atrium, left ventricle, and aorta during ventricular systole and diastole (see figure 12.19).
19. What events cause the first and second heart sounds?
20. Define murmur. Describe how either an incompetent or a stenosed valve can cause a murmur.
21. Define cardiac output, stroke volume, and heart rate.
22. What is Starling's law of the heart? What effect does an increase or a decrease in venous return have on cardiac output?
23. Describe the effect of parasympathetic and sympathetic stimulation on heart rate and stroke volume.

24. How does the nervous system detect and respond to the following?
    a. a decrease in blood pressure
    b. an increase in blood pressure
25. What is the effect of epinephrine on the heart rate and stroke volume?
26. Explain how emotions affect heart function.
27. What effects do the following have on cardiac output?
    a. a decrease in blood pH
    b. an increase in blood CO_2
28. How do changes in body temperature influence the heart rate?

CRITICAL THINKING

1. A friend tells you that an ECG revealed that her son has a slight heart murmur. Should you be convinced that he has a heart murmur? Explain.
2. Explain the effect on Starling's law of the heart if the parasympathetic (vagus) nerves to the heart are cut.
3. Describe the effect on heart rate if the sensory nerve fibers from the baroreceptors are cut.
4. An experiment is performed on a dog in which the arterial blood pressure in the aorta is monitored before and after the common carotid arteries are clamped. Explain the change in arterial blood pressure that would occur. (*Hint:* Baroreceptors are located in the internal carotid arteries, which are superior to the site of clamping of the common carotid arteries.)
5. What would be the effects on the heart if a person took a large dose of a drug that blocks calcium channels?
6. What happens to cardiac output following the ingestion of a large amount of fluid?
7. At rest, the cardiac output of athletes and nonathletes can be equal, but the heart rate of athletes is lower than that of nonathletes. At maximum exertion, the maximum heart rate of athletes and nonathletes can be equal, but the cardiac output of athletes is greater than that of nonathletes. Explain these differences.
8. Explain why it is useful that the walls of the ventricles are thicker than those of the atria.
9. Describe the effect of an incompetent aortic semilunar valve on ventricular and aortic pressure during ventricular systole and diastole.

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

13

Blood Vessels and Circulation

After passing from the right atrium to the right ventricle, blood is pumped into the pulmonary trunk. The pulmonary trunk divides into the right and left pulmonary arteries, which carry deoxygenated blood to the lungs. In the lung capillaries, CO^2 is given off, and the blood picks up O^2. Blood, now rich in O^2, flows from each lung to the left atrium. Blood passes from the left atrium to the left ventricle. The left ventricle then pumps the blood into the aorta, which distributes the oxygenated blood through its

branches to all of the body. Blood returns from the body to the right atrium through a series of venules and veins, and the cycle continues.

LEARN TO APPLY IT

T. J. and Tyler were building a treehouse. While searching for a board in a pile of lumber, T. J. stepped on a rusty nail that penetrated deep into his foot, causing it to bleed. Neither T. J. nor Tyler wanted to tell their parents about the accident, but after three days, T. J.'s foot became infected and the infection spread into his bloodstream. The infection quickly became much worse, and T. J. went into septic shock.

Explain how T. J.'s blood volume, blood pressure, heart rate, and stroke volume changed due to septic shock. Also, explain how blood flow in the periphery changed and how it affected T. J.'s appearance. Finally, explain the consequences if T. J.'s blood pressure remained abnormally low for a prolonged period of time.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 9 Cardiovascular System

13.1 FUNCTIONS OF THE CIRCULATORY SYSTEM

Learning Outcome *After reading this section, you should be able to*

A. List the functions of the circulatory system.

The blood vessels of the body form a network more complex than an interstate highway system. The blood vessels carry blood to within two or three cell diameters of nearly all the trillions of cells that make up the body. Blood flow through them is regulated, so that cells receive adequate nutrients and so that waste products are removed. Blood vessels remain functional, in most cases, in excess of 70 years. And like many other structures of the body, when blood vessels are damaged, they repair themselves.

Blood vessels outside the heart are divided into two classes: (1) the **pulmonary vessels,** which transport blood from the right ventricle of the heart through the lungs and back to the left atrium, and (2) the **systemic vessels,** which transport blood from the left ventricle of the heart through all parts of the body and back to the right atrium (see chapter 12 and figure 12.2).

Together, the pulmonary vessels and the systemic vessels constitute the *circulatory system*.

Blood flow through the circulatory system is ensured by the pumping action of the heart. On its own, the circulatory system has five functions:

1. *Carries blood.* Blood vessels carry blood from the heart to all the tissues of the body and back to the heart.
2. *Exchanges nutrients, waste products, and gases with tissues.* Nutrients and O_2 diffuse from blood vessels to cells in essentially all areas of the body. Waste products and CO_2 diffuse from the cells, where they are produced, to blood vessels.
3. *Transports substances.* Blood transports hormones, components of the immune system, molecules required for coagulation, enzymes, nutrients, gases, waste products, and other substances to and from all areas of the body.
4. *Helps regulate blood pressure.* The circulatory system and the heart work together to regulate blood pressure within a normal range.
5. *Directs blood flow to the tissues.* The circulatory system directs blood to tissues when increased blood flow is required to maintain homeostasis.

13.2 GENERAL FEATURES OF BLOOD VESSEL STRUCTURE

Learning Outcome ***After reading this section, you should be able to***

A. Describe the structure and function of arteries, capillaries, and veins.

The three main types of blood vessels are (1) arteries, (2) capillaries, and (3) veins. **Arteries** (AR-ter-ees) carry blood away from the heart; usually, the blood is *oxygenated* (oxygen-rich). Blood is pumped from the ventricles of the heart into large, elastic arteries, which branch repeatedly to form progressively smaller arteries. As they become smaller, the artery walls undergo a gradual transition from having more elastic tissue than smooth muscle to having more smooth muscle than elastic tissue (figure 13.1*a*–*c*). The arteries are normally classified in one of three categories: (1) elastic arteries, (2) muscular arteries, or (3) arterioles. The various arteries form a continuum from the largest elastic arteries to the smallest arterioles.

Figure 13.1 APR **Blood Vessel Structure**

With the exception of capillaries and venules, blood vessel walls consist of three layers, or tunics: the outer tunica adventitia, the middle tunica media, and the inner tunica intima.

Blood flows from arterioles into **capillaries** (KAP-i-lair-ees). It is at the capillaries where exchange of substances such as O_2, nutrients, CO_2, and

other waste products occurs between the blood and the tissue fluid. Capillaries have thinner walls than do arteries (figure 13.1*d*). Blood flows through capillaries more slowly, and there are far more of them than of any other blood vessel type.

From the capillaries, blood flows into veins. **Veins** (VANES) carry blood toward the heart; usually, the blood is *deoxygenated* (oxygen-poor). Compared to arteries, the walls of veins are thinner and contain less elastic tissue and fewer smooth muscle cells (figure 13.1*e–g*). Starting at capillaries and proceeding toward the heart, small-diameter veins come together to form larger-diameter veins, which are fewer in number. Veins increase in diameter and decrease in number as they progress toward the heart, and their walls increase in thickness. Veins may be classified, from smallest to largest, as (1) venules, (2) small veins, (3) medium-sized veins, or (4) large veins.

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Except in capillaries and venules, blood vessel walls consist of three layers, or **tunics** (TOO-niks). From the inner to the outer wall, the tunics are (1) the tunica intima, (2) the tunica media, and (3) the tunica adventitia, or tunica externa (figure 13.2; see figure 13.1).

Figure 13.2 APR **Photomicrograph of an Artery and a Vein**

The typical structure of a medium-sized artery (A) and vein (V). Note that the artery has a thicker wall than the vein. The predominant layer in the wall of the artery is the tunica media with its circular layers of smooth muscle. The predominant layer in the wall of the vein is the tunica adventitia, and the tunica media is thinner.

Ed Reschke/Photolibrary/Getty Images

The **tunica intima** (TOO-ni-kah IN-ti-mah), or innermost layer, consists of an **endothelium** (en-doh-THEE-lee-um), composed of simple squamous epithelial cells, a basement membrane, and a small amount of connective tissue. In muscular arteries, the tunica intima also contains a layer of thin elastic connective tissue. The **tunica media,** or middle layer, consists of smooth muscle cells arranged circularly around the blood vessel. It also contains variable amounts of elastic and collagen fibers, depending on the size and type of the vessel. In muscular arteries, a layer of elastic connective tissue forms the outer margin of the tunica media. The **tunica adventitia** (TOO-ni-kah ad-ven-TISH-ah) is composed of dense connective tissue adjacent to the tunica media; the tissue becomes loose connective tissue toward the outer portion of the blood vessel wall.

Arteries

Elastic arteries are the largest-diameter arteries and have the thickest walls (see figure 13.1*a*). Compared to other arteries, a greater proportion of their walls is composed of elastic tissue, and a smaller proportion is smooth muscle. The aorta and pulmonary trunk are examples of elastic arteries. Elastic arteries stretch when the ventricles of the heart pump blood into them. The elastic recoil of these arteries prevents blood pressure from falling rapidly and maintains blood flow while the ventricles are relaxed.

The **muscular arteries** include medium-sized and small arteries. The walls of medium-sized arteries are relatively thick compared to their diameter. Most of the wall's thickness is from smooth muscle cells of the tunica media (see figure 13.1*b*). Medium-sized arteries are frequently called **distributing arteries** because the smooth muscle tissue enables these vessels to control blood flow to different body regions. Contraction of the smooth muscle in blood vessels, called **vasoconstriction** (VAY-soh-con-STRIK-shun), decreases blood vessel diameter and blood flow. Relaxation of the smooth muscle in blood vessels, called **vasodilation** (VAY-soh-die-LAY-shun), increases blood vessel diameter and blood flow.

Medium-sized arteries supply blood to small arteries. Small arteries have about the same structure as the medium-sized arteries, except for a smaller diameter and thinner walls. The smallest of the small arteries have only three or four layers of smooth muscle in their walls.

Arterioles (ar-TEER-ee-oles) transport blood from small arteries to capillaries. Arterioles (see figure 13.1*c*) are the smallest arteries in which the three tunics can be identified. The tunica media of arterioles consists of only

one or two layers of circular smooth muscle cells. Small arteries and arterioles are adapted for vasodilation and vasoconstriction.

Capillaries

Blood flows from arterioles into capillaries. Capillaries branch to form networks (figure 13.3; see figure 13.1*d*). Blood flow through capillary networks is regulated by smooth muscle cells called **precapillary sphincters.** These precapillary sphincters are located at the origin of the branches of the capillaries and, by contracting and relaxing, regulate the amount of blood flow through the various sections of the network.

Figure 13.3 **Capillary Network**

A capillary network stems from an arteriole. The network forms numerous branches. Blood flows through capillaries into venules. Smooth muscle cells, called precapillary sphincters, regulate blood flow through the capillaries. Blood flow decreases when the precapillary sphincters constrict and increases when they dilate.

Capillary walls are very thin and consist only of endothelium. The thin walls of capillaries facilitate diffusion between the capillaries and surrounding cells. Each capillary is 0.5–1 millimeter (mm) long. Capillaries branch without changing their diameter, which is approximately the same as the diameter of a red blood cell (7.5 μm).

Red blood cells flow through most capillaries in single file and are frequently folded as they pass through the smaller-diameter capillaries. As blood flows through capillaries, blood gives up O_2 and nutrients to the tissue

spaces and takes up CO_2 and other by-products of metabolism. Capillary networks are more numerous and more extensive in the lungs and in highly metabolic tissues, such as the liver, kidneys, skeletal muscle, and cardiac muscle, than in other tissue types.

Veins

Blood flows from capillaries into venules and from venules into small veins. **Venules** (VEN-yools) have a diameter slightly larger than that of capillaries and are composed of endothelium resting on a delicate connective tissue layer (see figure 13.1*e*). The structure of venules, except for their diameter, is very similar to that of capillaries. Small veins are slightly larger in diameter than venules. All three tunics are present in small veins. The tunica media contains a continuous layer of smooth muscle cells, and the connective tissue of the tunica adventitia surrounds the tunica media (see figure 13.1*f*).

Medium-sized veins collect blood from small veins and deliver it to large veins. The three thin but distinctive tunics make up the wall of the medium-sized and large veins. The tunica media contains some circular smooth muscle and sparsely scattered elastic fibers. The predominant layer in veins is the outer tunica adventitia, which consists primarily of dense collagen fibers (see figures 13.1*g* and 13.2). Consequently, veins are more distensible than arteries. The connective tissue of the tunica adventitia determines the degree to which they can distend.

Veins that have diameters greater than 2 mm contain **valves,** which ensure that blood flows toward the heart but not in the opposite direction (figure 13.4). Each valve consists of folds in the tunica intima that form two flaps. These valves are similar in shape and function to the semilunar valves of the heart. There are many valves in medium-sized veins and more valves in veins of the lower limbs than in veins of the upper limbs. This prevents blood from flowing toward the feet in response to the pull of gravity.

Figure 13.4 **Valves**

Folds in the tunica intima form the valves of veins, which allow blood to flow toward the heart but not in the opposite direction.

CLINICAL IMPACT

Varicose Veins

Varicose (VAIR-ih-kos) **veins** result when the veins of the lower limbs become so dilated that the cusps of the valves no longer overlap to prevent the backflow of blood. As a consequence, venous pressure is greater than normal in the veins of the lower limbs and can result in edema (swelling) of the limb. Some people have a genetic tendency to develop varicose veins. The condition is further encouraged by activities that increase the pressure in veins. For example, standing in place for prolonged periods allows the pressure of the blood to stretch the veins, and the enlarged uterus in pregnancy compresses the veins in the pelvis, increasing pressure in the veins that drain the lower limbs.

The blood in varicose veins can become so stagnant that it clots. The clots, called **thromboses,** can cause inflammation of the veins, a condition called **phlebitis** (fleh-BIE-tis). If the condition becomes severe enough, the blocked veins can prevent blood from flowing through the capillaries that are drained by the veins. The lack of blood flow can lead to tissue death and infection with anaerobic bacteria, a condition called **gangrene** (GANG-green). In addition, fragments of the clots may dislodge and travel through the veins to the lungs, where they can cause severe damage. Fragments of thromboses that dislodge and float in the blood are called **emboli** (EM-boh-lie).

13.3 BLOOD VESSELS OF THE PULMONARY CIRCULATION

Learning Outcome *After reading this section, you should be able to*

A. Describe the blood vessels of the pulmonary circulation.

The **pulmonary circulation** is the system of blood vessels that carries blood from the right ventricle of the heart to the lungs and back to the left atrium of the heart. Blood from the right ventricle is pumped into a short vessel called the **pulmonary trunk** (figure 13.5). The pulmonary trunk then branches into the **right** and **left pulmonary arteries,** which extend to the right and left lungs, respectively. These arteries carry deoxygenated blood to the pulmonary capillaries in the lungs, where the blood takes up O_2 and releases CO_2. Oxygenated blood then flows from the lungs to the left atrium. Four **pulmonary veins** (two from each lung) exit the lungs and carry the oxygenated blood to the left atrium. The chapter 13 opening figure as well as figure 12.2 illustrate the path of the pulmonary circulation and show it in relation to the systemic circulation, described next.

Figure 13.5 APR **Major Arteries**

These major arteries carry blood from the left ventricle of the heart to the body tissues.

13.4 BLOOD VESSELS OF THE SYSTEMIC CIRCULATION: ARTERIES

Learning Outcome *After reading this section, you should be able to*

A. List the major arteries that supply each of the body areas, and describe their functions.

The **systemic circulation** is the system of blood vessels that carries blood from the left ventricle of the heart to the tissues of the body and back to the right atrium. Oxygenated blood from the pulmonary veins passes from the left atrium into the left ventricle and from the left ventricle into the aorta. Arteries distribute blood from the aorta to all portions of the body (figure 13.5).

Aorta

All arteries of the systemic circulation branch directly or indirectly from the **aorta** (ay-OR-tuh). The aorta is usually considered in three parts—(1) the ascending aorta, (2) the aortic arch, and (3) the descending aorta. The descending aorta is further divided into the thoracic aorta and the abdominal aorta (figure 13.6*a*).

Figure 13.6 APR **Branches of the Aorta**

(*a*) The aorta is considered in three portions: the ascending aorta, the aortic arch, and the descending aorta. The descending aorta consists of the thoracic aorta and the abdominal aorta. (*b*) The thoracic aorta. (*c*) The abdominal aorta.

The **ascending aorta** is the part of the aorta that passes superiorly from the left ventricle. The right and left **coronary arteries** arise from the base of the ascending aorta and supply blood to the heart (see chapter 12).

The aorta arches posteriorly and to the left as the **aortic arch.** Three major arteries, which carry blood to the head and upper limbs, originate from the aortic arch: (1) the brachiocephalic artery, (2) the left common carotid artery, and (3) the left subclavian artery (figure 13.6*b*).

The **descending aorta** is the longest part of the aorta. It extends through the thorax and abdomen to the upper margin of the pelvis. The part of the descending aorta that extends through the thorax to the diaphragm is called the **thoracic** (thor-ASS-ik) **aorta.** The part of the descending aorta that extends from the diaphragm to the point at which it divides into the two **common iliac** (IL-ee-ack) **arteries** is called the **abdominal** (ab-DOM-i-nal) **aorta** (figure 13.6*a*, *c*).

An **arterial aneurysm** (AN-you-rizm; a dilation) is a localized dilation of an artery that usually develops in response to trauma or a congenital (existing at birth) weakness of the artery wall. Rupture of a large aneurysm in the aorta is almost always fatal, and rupture of an aneurysm in an artery of the brain causes massive damage to brain tissue and even death. If aneurysms are discovered, they can sometimes be surgically corrected. For example, large aortic aneurysms that leak blood slowly can often be repaired.

Arteries of the Head and Neck

Figure 13.7 depicts the arteries of the head and neck. The first vessel to branch from the aortic arch is the **brachiocephalic** (BRAH-kee-oh-se-FAL-ik; vessel to the arm and head) **artery**. This artery extends a short distance and then branches at the level of the clavicle to form the **right common carotid** (kah-ROT-id) **artery,** which transports blood to the right side of the head and neck, and the **right subclavian** (sub-KLAY-vee-an; beneath the clavicle) **artery**, which transports blood to the right upper limb (see figures 13.6*b* and 13.7).

Figure 13.7 APR **Arteries of the Head and Neck**

The brachiocephalic artery, the right common carotid artery, and the right vertebral artery supply the head and neck. The right common carotid artery branches from the brachiocephalic artery, and the vertebral artery branches from the subclavian artery.

There is no brachiocephalic artery on the left side of the body. Instead, both the left common carotid and the left subclavian arteries branch directly off the aortic arch (see figures 13.5, 13.6*a*, *b*). They are the second and third branches of the aortic arch. The **left common carotid artery** transports blood to the left side of the head and neck, and the **left subclavian artery** transports blood to the left upper limb.

The common carotid arteries extend superiorly along each side of the neck to the angle of the mandible, where they branch into **internal** and **external carotid arteries.** The base of each internal carotid artery is slightly dilated to form a **carotid sinus,** which contains structures important in monitoring blood pressure (baroreceptors). The external carotid arteries have several branches that supply the structures of the neck, face, nose, and mouth. The internal carotid arteries pass through the carotid canals and contribute to the

cerebral arterial circle (circle of Willis) at the base of the brain (figure 13.8). The vessels that supply blood to most of the brain branch from the cerebral arterial circle.

Figure 13.8 APR **Cerebral Arterial Circle**

The internal carotid and vertebral arteries carry blood to the brain. The vertebral arteries join to form the basilar artery. Branches of the internal carotid arteries and the basilar artery supply blood to the brain and complete a circle of arteries around the pituitary gland and the base of the brain called the cerebral arterial circle (circle of Willis).

Some of the blood to the brain is supplied by the **vertebral** (VER-tee-bral) **arteries,** which branch from the subclavian arteries and pass to the head through the transverse foramina of the cervical vertebrae (see figure 13.7). The vertebral arteries then pass into the cranial cavity through the foramen magnum. Branches of the vertebral arteries supply blood to the spinal cord, as well as to the vertebrae, muscles, and ligaments in the neck.

Within the cranial cavity, the vertebral arteries unite to form a single **basilar** (BAS-ih-lar; relating to the base of the brain) **artery** Within the cranial cavity, the vertebral arteries unite to form a single **basilar** located along the anterior, inferior surface of the brainstem (figure 13.8). The basilar artery gives off branches that supply blood to the pons, cerebellum, and midbrain. It also forms right and left branches that contribute to the cerebral arterial circle. Most of the blood supply to the brain is through the internal

carotid arteries; however, not enough blood is supplied to the brain to maintain life if either the vertebral arteries or the carotid arteries are blocked.

Apply It 1

The term carotid means to put to sleep, reflecting the fact that, if the carotid arteries are blocked for several seconds, the patient can lose consciousness. Interruption of the blood supply for even a few minutes can result in permanent brain damage. What is the physiological significance of atherosclerosis (lipid deposits that block the vessels) in the carotid arteries?

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Arteries of the Upper Limbs

The arteries of the upper limbs are named differently as they pass into different body regions, even though no major branching occurs. The subclavian artery, located deep to the clavicle, becomes the **axillary** (AK-sil-air-ee) **artery** in the axilla (armpit). When the axillary artery extends into the arm, it is then referred to as the **brachial** (BRAY-kee-al) **artery** (figure 13.9). Blood pressure measurements are normally taken from the brachial artery. The brachial artery branches at the elbow to form the **ulnar** (UL-nair) **artery** and the **radial** (RAY-dee-al) **artery,** which supply blood to the forearm and hand. The radial artery is the one most commonly used for taking a pulse. The pulse can be detected easily on the thumb (radial) side of the anterior surface of the wrist.

Figure 13.9 APR **Arteries of the Upper Limb**
Anterior view of the arteries of the right upper limb and their branches.

Thoracic Aorta and Its Branches

The branches of the thoracic aorta can be divided into two groups: (1) the **visceral** (VISS-er-al) **arteries** and (2) the **parietal** (pah-RYE-eh-tal) **arteries.** The visceral arteries supply blood to thoracic organs, including the esophagus, the trachea, the parietal pericardium, and part of the lung. The parietal arteries supply blood to the thoracic wall, and include the **posterior intercostal** (in-ter-KOS-tal) **arteries,** which arise from the thoracic aorta and extend between the ribs (see figure 13.6*a*, *b*). They supply the intercostal muscles, the vertebrae, the spinal cord, and the deep muscles of the back. The **superior phrenic** (FREN-ik; diaphragm) **arteries** supply the diaphragm.

The **internal thoracic arteries** are branches of the subclavian arteries. They descend along the internal surface of the anterior thoracic wall and give rise to branches called the **anterior intercostal arteries,** which extend between the ribs to supply the anterior chest wall (see figure 13.6*a*, *b*).

Abdominal Aorta and Its Branches

The branches of the abdominal aorta, like those of the thoracic aorta, can be divided into visceral and parietal groups. The visceral arteries are divided into paired and unpaired branches. There are three major unpaired visceral artery branches: (1) the **celiac** (SEE-lee-ak; belly) **trunk,** (2) the **superior mesenteric** (mes-en-TER-ik) **artery,** and (3) the **inferior mesenteric artery.** The celiac trunk supplies blood to the stomach, pancreas, spleen, upper duodenum, and liver. The superior mesenteric artery supplies blood to the small intestine and the upper portion of the large intestine, and the inferior mesenteric artery supplies blood to the remainder of the large intestine (see figure 13.6*c*).

There are three paired visceral branches of the abdominal aorta: (1) the renal arteries, (2) the suprarenal arteries, and (3) the gonadal arteries. The **renal** (REE-nal; kidney) **arteries** supply the kidneys, and the **suprarenal** (SOO-prah-REE-nal; superior to the kidney) **arteries** supply the adrenal glands. The gonadal arteries supply the reproductive organs. Specifically, the **testicular arteries** supply the testes in males: and the **ovarian arteries** supply the ovaries in females.

The parietal branches of the abdominal aorta supply the diaphragm and abdominal wall. The **inferior phrenic arteries** supply the diaphragm; the **lumbar arteries** supply the lumbar vertebrae and back muscles; and the **median sacral artery** supplies the inferior vertebrae.

Arteries of the Pelvis

The abdominal aorta divides at the level of the fifth lumbar vertebra into two **common iliac arteries.** Each common iliac artery extends a short distance and then divides to form an **external iliac artery,** which enters a lower limb, and an **internal iliac artery,** which supplies the pelvic area (see figure 13.6*c*). Visceral branches of the internal iliac artery supply organs such as the urinary bladder, rectum, uterus, and vagina. Parietal branches supply blood to the walls and floor of the pelvis; the lumbar, gluteal, and proximal thigh muscles; and the external genitalia.

Arteries of the Lower Limbs

Like the arteries of the upper limbs, the arteries of the lower limbs are named differently as they pass into different body regions, even though there are no major branches. The external iliac artery in the pelvis becomes the **femoral** (FEM-o-ral) **artery** in the thigh. The femoral artery extends down the thigh and becomes the **popliteal** (pop-LIT-ee-al) **artery** in the popliteal space,

which is the posterior region of the knee. The popliteal artery branches slightly inferior to the knee to give off the **anterior tibial artery** and the **posterior tibial artery,** both of which give rise to arteries that supply blood to the leg and foot (figure 13.10). The anterior tibial artery becomes the **dorsalis pedis** (door-SAL-lis PEE-dis; *pes,* foot) **artery** at the ankle. The posterior tibial artery gives rise to the **fibular artery,** or *peroneal artery,* which supplies the lateral leg and foot.

Figure 13.10 APR **Arteries of the Lower Limb**
Anterior view of the arteries of the right lower limb and their branches.

The femoral triangle is located in the superior and medial area of the thigh. Its margins are formed by the inguinal ligament, the medial margin of the sartorius muscle, and the lateral margin of the adductor longus muscle (see figures 7.15*a* and 7.25*a*). Passing through the femoral triangle are the femoral artery, vein, and nerve. A pulse in the femoral artery can be detected in the

area of the femoral triangle. This area is also susceptible to serious traumatic injuries that result in hemorrhage and nerve damage. In addition, pressure applied to this area can help prevent bleeding from wounds in more distal areas of the lower limb. The femoral triangle is an important access point for certain medical procedures as well.

13.5 BLOOD VESSELS OF THE SYSTEMIC CIRCULATION: VEINS

Learning Outcome *After reading this section, you should be able to*

A. List the major veins that carry blood from each of the body areas, and describe their functions.

The deoxygenated blood from the tissues of the body returns to the heart through veins. The **superior vena cava** (VEE-nah KAY-vah) returns blood from the head, neck, thorax, and upper limbs to the right atrium of the heart, and the **inferior vena cava** returns blood from the abdomen, pelvis, and lower limbs to the right atrium (figure 13.11).

Figure 13.11 APR **Major Veins**

These major veins return blood from the body tissues to the right atrium.

Veins of the Head and Neck

The two pairs of major veins that collect blood from the head and neck are (1) the **external jugular** (JUG-you-lar) **veins** and (2) the **internal jugular veins** (figure 13.12). The external jugular veins are the more superficial of the two sets. They carry blood from the posterior head and neck, emptying primarily into the subclavian veins. The internal jugular veins are much larger and deeper. They carry blood from the brain and the anterior head, face, and neck. The internal jugular veins join the **subclavian veins** on each side of the body to form the **brachiocephalic veins.** The brachiocephalic veins join to form the superior vena cava.

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Figure 13.12 APR **Veins of the Head and Neck**

The external and internal jugular veins drain blood from the head and neck. The internal jugular veins join the subclavian veins on each side of the body to form the brachiocephalic veins. The external jugular veins drain into the subclavian veins.

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Veins of the Upper Limbs

The veins of the upper limbs (figure 13.13) can be divided into deep and superficial groups. The deep veins, which carry blood from the deep structures of the upper limbs, follow the same course as the arteries and are named for their respective arteries. The major deep veins are the **brachial veins,** which accompany the brachial artery and empty into the axillary vein. The superficial veins carry blood from the superficial structures of the upper limbs and then empty into the deep veins. The **cephalic** (SE-FAL-ik; toward the head) **vein,** which empties into the **axillary vein,** and the **basilic** (ba-SIL-ik) **vein,** which becomes the axillary vein, are the major superficial veins. Many of their tributaries in the forearm and hand can be seen through the skin. The **median cubital** (KYOO-bi-tal) **vein** usually connects the cephalic vein or its tributaries with the basilic vein. Although this vein varies in size among people, it is usually quite prominent on the anterior surface of the upper limb at the level of the elbow, an area called the **cubital fossa,** and is often used as a site for drawing blood.

Figure 13.13 APR **Veins of the Upper Limb**
Anterior view of the major veins of the right upper limb and their branches.

Veins of the Thorax

Three major veins return blood from the thorax to the superior vena cava: (1) the **right brachiocephalic vein,** (2) the **left brachiocephalic vein** and (3) the **azygos** (az-IH-gos, AZ-i-gos) **vein** (figure 13.14). Blood returns from the anterior thoracic wall by way of the **anterior intercostal veins.** These veins empty into the **internal thoracic veins,** which empty into the brachiocephalic veins. Blood from the posterior thoracic wall is collected by **posterior intercostal veins** that empty into the azygos vein on the right and the **hemiazygos vein** or the **accessory hemiazygos vein** on the left. The hemiazygos and accessory hemiazygos veins empty into the azygos vein, which empties into the superior vena cava (see figure 13.12).

Figure 13.14 APR **Veins of the Thorax**
Anterior view of veins of the thorax.

Veins of the Abdomen and Pelvis

Blood from the posterior abdominal wall returns toward the heart through **ascending lumbar veins** into the azygos vein. Blood from the rest of the abdomen and from the pelvis and lower limbs returns to the heart through the inferior vena cava. The gonads (testes or ovaries), kidneys, adrenal glands, and liver are the only abdominal organs outside the pelvis from which blood empties directly into the inferior vena cava. The **internal iliac veins** return blood from the pelvis and join the **external iliac veins** from the lower limbs

to form the **common iliac veins.** The common iliac veins combine to form the inferior vena cava (see figure 13.11).

The liver is a major processing center for substances absorbed by the intestinal tract. As such, blood from the capillaries within most of the abdominal viscera, such as the stomach, intestines, pancreas, and spleen, drains through a specialized portal system to the liver. A **portal** (POR-tal) **system** is a system of blood vessels that begins and ends with capillary beds and has no pumping mechanism, such as the heart, in between. The **hepatic** (hep-AT-ik) **portal system** (figure 13.15) begins with capillaries in the viscera and ends with capillaries in the liver. The major vessels of the hepatic portal system are the **splenic** (SPLEN-ik) **vein** and the **superior mesenteric vein.** The **inferior mesenteric vein** empties into the splenic vein. The splenic vein carries blood from the spleen and pancreas. The superior and inferior mesenteric veins carry blood from the intestines. The splenic vein and the superior mesenteric vein join to form the **hepatic portal vein,** which enters the liver.

Figure 13.15 APR **Veins of the Hepatic Portal System**

The hepatic portal system begins as capillary beds in the stomach, pancreas, spleen, small intestine, and large intestine. The veins of the hepatic portal system converge on the hepatic portal vein, which carries blood to a series of capillaries in the liver. Hepatic veins carry blood from capillaries in the liver to the hepatic veins, which then enter the inferior vena cava.

CLINICAL IMPACT

Blood Vessels Used for Coronary Bypass Surgery

The great saphenous vein is often surgically removed and used in coronary bypass surgery. Portions of the saphenous vein are grafted to create a route for blood flow that bypasses blocked portions of the coronary arteries. The circulation interrupted by the removal of the saphenous vein flows through other veins of the lower limb instead. The internal thoracic artery is also used for coronary bypasses. The distal end of the artery is freed and attached to a coronary artery at a point that bypasses the blocked portion. This technique appears to be better because the internal thoracic artery does not become blocked as fast as the saphenous vein. However, due to the length of the saphenous vein and the fact that more than one segment can be removed for use in bypass surgery, surgeons use the saphenous vein.

Blood from the liver flows into **hepatic veins,** which join the inferior vena cava. Blood entering the liver through the hepatic portal vein is rich in nutrients collected from the intestines, but it may also contain a number of toxic substances that are potentially harmful to body tissues. Within the liver, nutrients are taken up and stored or modified, so that they can be used by other cells of the body. Also within the liver, toxic substances are converted to nontoxic substances. These substances can be removed from the blood or carried by the blood to the kidneys for excretion. The liver is discussed more fully in chapter 16.

Other veins of the abdomen and pelvis include the renal veins, the suprarenal veins, and the gonadal veins. The **renal veins** carry blood from the kidneys, and the **suprarenal veins** drain the adrenal glands. The gonadal veins drain blood from the reproductive organs. Specifically, the **testicular**

veins drain the testes in males and the **ovarian veins** drain the ovaries in females.

Veins of the Lower Limbs

The veins of the lower limbs (figure 13.16), like those of the upper limbs, consist of deep and superficial groups. The deep veins follow the same path as the arteries and are named for the arteries they accompany. The superficial veins consist of the great and small **saphenous** (sah-FEE-nus, SA-feh-nus) **veins.** The **great saphenous vein** originates over the dorsal and medial side of the foot and ascends along the medial side of the leg and thigh to empty into the femoral vein. The **small saphenous vein** begins over the lateral side of the foot and joins the **popliteal vein,** which becomes the femoral vein. The femoral vein empties into the external iliac vein.

Figure 13.16 APR **Veins of the Lower Limb**

Anterior view of the major veins of the right lower limb and their branches.

Apply It 2

If a thrombus in the posterior tibial vein gave rise to an embolus, name in order the parts of the circulatory system the embolus would pass through before lodging in a blood vessel in the lungs. Why are the lungs the most likely place for the embolus to lodge?

13.6 PHYSIOLOGY OF CIRCULATION

Learning Outcomes *After reading this section, you should be able to*

A. Explain how blood pressure and resistance to flow change as blood flows through the blood vessels.

B. Describe the exchange of material across a capillary wall.

The function of the circulatory system is to maintain adequate blood flow to all body tissues. Adequate blood flow is required to provide nutrients and O_2 to the tissues and to remove the waste products of metabolism from the tissues. Blood flows through the arterial system primarily as a result of the pressure produced by contractions of the heart ventricles.

Blood Pressure

Blood pressure is a measure of the force blood exerts against the blood vessel walls. In arteries, blood pressure values go through a cycle that depends on the rhythmic contractions of the heart. When the ventricles contract, blood is forced into the arteries, and the pressure reaches a maximum value called the **systolic pressure**. When the ventricles relax, blood pressure in the arteries falls to a minimum value called the **diastolic pressure**. The standard unit for measuring blood pressure is millimeters of mercury (mm Hg). For example, if the blood pressure is 100 mm Hg, the pressure is great enough to lift a column of mercury 100 mm.

Health professionals most often use the **auscultatory** (AW-skul-ta-to-ree; to listen) method to determine blood pressure. Figure 13.17 illustrates the mechanism by which blood pressure is determined using this method.

PROCESS Figure

PROCESS Figure 13.17 **Measuring Blood Pressure**

The auscultatory method, demonstrated in this figure, allows health professionals to measure arterial blood pressure.

When the pressure cuff is inflated to close the brachial artery, which arteries will not receive blood flow?

❶ A blood pressure cuff connected to a **sphygmomanometer** (SFIG-moh-mah-NOM-ih-ter) is wrapped around the patient's arm, and a **stethoscope** (STETH-oh-skope) is placed over the brachial artery. The blood pressure cuff is then inflated until the brachial artery is completely blocked.

❷ Because no blood flows through the constricted area at this point, no sounds can be heard through the stethoscope.

❸ The pressure in the cuff is then gradually lowered. As soon as the pressure in the cuff declines below the systolic pressure, blood flows through the

constricted area each time the left ventricle contracts. The blood flow is turbulent immediately downstream from the constricted area. This turbulence produces vibrations in the blood and surrounding tissues that can be heard through the stethoscope. These sounds are called **Korotkoff** (koh-ROT-kof) **sounds,** and the pressure at which the first Korotkoff sound is heard is the systolic pressure.

4. As the pressure in the blood pressure cuff is lowered still more, the Korotkoff sounds change tone and loudness.
5. When the pressure has dropped until the brachial artery is no longer constricted and blood flow is no longer turbulent, the sound disappears completely. The pressure at which the Korotkoff sounds disappear is the diastolic pressure. The brachial artery remains open during systole and diastole, and continuous blood flow is reestablished.

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CLINICAL IMPACT

Hypertension

Hypertension, or *high blood pressure,* affects at least 20% of all people at some time in their lives. The following guidelines categorize blood pressure for adults:

- *Normal:* less than 120 mm Hg systolic and 80 mm Hg diastolic
- *Prehypertension:* from 120 mm Hg systolic and 80 mm Hg diastolic to 139 mm Hg systolic and 89 mm Hg diastolic
- *Stage 1 hypertension:* from 140 mm Hg systolic and 90 mm Hg diastolic to 159 mm Hg systolic and 99 mm Hg diastolic
- *Stage 2 hypertension:* greater than 160 mm Hg systolic and 100 mm Hg diastolic

Individuals with prehypertension pressure should monitor their blood pressure regularly and consider lifestyle changes that can reduce blood pressure.

Hypertension requires the heart to perform a greater-than-normal amount of work because of the increased afterload (see chapter 12). The extra work leads to hypertrophy of cardiac muscle, especially in the left ventricle, and can result in heart failure. Hypertension also increases the rate of arteriosclerosis development. Arteriosclerosis, in turn, increases the chance that blood clots will form and that blood vessels will rupture. Common conditions associated with hypertension are cerebral hemorrhage, heart attack, hemorrhage of renal blood vessels, and poor vision resulting from burst blood vessels in the retina.

The most common treatments for hypertension are those that dilate blood vessels, increase the rate of urine production, or decrease cardiac output. A low-salt diet is also recommended to reduce the amount of sodium chloride and water absorbed from the intestine into the bloodstream.

Source: Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.

The systolic pressure is the maximum pressure produced in the large arteries. It is also a good measure of the maximum pressure within the left ventricle. The diastolic pressure is close to the lowest pressure within the large arteries. During relaxation of the left ventricle, the aortic semilunar valve closes, trapping the blood that was ejected during ventricular contraction in the aorta. The pressure in the ventricles falls to 0 mm Hg during ventricular relaxation. However, the blood trapped in the elastic arteries is compressed by the recoil of the elastic arteries, and the pressure falls more slowly, reaching the diastolic pressure (see figure 12.19).

Pressure and Resistance

The values for systolic and diastolic pressure vary among healthy people, making the range of normal values quite broad. In addition, other factors, such as physical activity and emotions, affect blood pressure values in a normal person. A standard blood pressure for a resting young adult male is 120 mm Hg for the systolic pressure and 80 mm Hg for the diastolic pressure, commonly expressed as 120/80.

As blood flows from arteries through the capillaries and veins, blood pressure falls progressively to about 0 mm Hg or even slightly lower by the time blood is returned to the right atrium. In addition, the fluctuations in blood pressure are damped, meaning that the difference between the systolic and diastolic pressures is decreased in the small-diameter vessels. The decrease in fluctuations in pressure is the result of increased resistance to blood flow in smaller and smaller vessels. By the time blood reaches the capillaries, the smallest of the vessels, there is no variation in blood pressure, and only a steady pressure of about 30 mm Hg remains (figure 13.18).

Figure 13.18 **Blood Pressure in the Various Blood Vessel Types**

In small arteries and arterioles, blood pressure fluctuations between systole and diastole are damped, so the fluctuations become smaller. No fluctuations in blood pressure occur in capillaries and veins.

Resistance to blood flow is related to the diameter of the blood vessel. The smaller the diameter of the blood vessel, the greater the resistance to flow. As a consequence of this greater resistance to flow, there is also a more rapid decrease in pressure as blood flows through smaller vessels. The most rapid decline in blood pressure occurs in the arterioles and capillaries because their small diameters increase the resistance to blood flow. Blood pressure declines slowly as blood flows from large to medium-sized arteries because their diameters are larger and the resistance to blood flow is not as great.

Because of veins' large diameters, resistance to blood flow in them is low. The low resistance results in low blood pressure in the veins. However, though pressure is low, blood continues to flow through the veins toward the heart. Blood flow rate is ensured and amplified by valves that prevent the backflow of blood in the veins, as well as skeletal muscle movements that periodically compress veins, forcing blood to flow toward the heart.

The muscular arteries, arterioles, and precapillary sphincters are capable of constricting (vasoconstriction) and dilating (vasodilation). Resistance to blood flow increases as vessels constrict and the volume of blood flowing

through the vessels declines. Because muscular arteries are able to constrict and dilate, they help control the amount of blood flowing to each region of the body. At a finer level, arterioles and precapillary sphincters regulate blood flow through local tissues (see figure 13.3).

Pulse Pressure

The difference between the systolic and diastolic pressures is called the **pulse pressure.** For example, if a person has a systolic pressure of 120 mm Hg and a diastolic pressure of 80 mm Hg, the pulse pressure is 40 mm Hg (120 – 80 = 40). Two factors affect pulse pressure: (1) stroke volume and (2) vascular compliance. When the stroke volume increases, the systolic pressure increases more than the diastolic pressure. This leads to a higher pulse pressure. During periods of exercise, the stroke volume and pulse pressure increase substantially.

Vascular compliance is related to the elasticity of the blood vessel wall. In people who have **arteriosclerosis** (ar-TEER-ee-oh-skler-OH-sis; hardening of the arteries), the arteries are less elastic than normal. Arterial pressure increases rapidly and falls rapidly in these less elastic arteries. The effect that this change has on blood pressure is that the systolic pressure increases substantially, and the diastolic pressure may be somewhat lower than normal or slightly increased. The same amount of blood ejected into a less elastic artery results in a higher systolic pressure than it would have in a more elastic artery. Therefore, the pulse pressure is greater than normal, even though the same amount of blood is ejected into the aorta as in a normal person. Arteriosclerosis increases the amount of work the heart performs because the left ventricle must produce a greater pressure to eject the same amount of blood into a less elastic artery. In severe cases, the heart's increased workload leads to heart failure.

Ejection of blood from the left ventricle into the aorta produces a pressure wave, or **pulse,** which travels rapidly along the arteries. A pulse can be felt at locations where large arteries are close to the surface of the body (figure 13.19). Health professionals should know the major locations of pulse detection because monitoring the pulse can yield important information about the heart rate, the heart rhythm, and other characteristics. For example, a weak pulse usually indicates a decreased stroke volume or increased constriction of the arteries.

Figure 13.19 **Major Points at Which the Pulse Can Be Monitored**
Each pulse point is named after the artery on which it occurs.

Apply It 3

A weak pulse occurs in response to premature heartbeats and during cardiovascular shock due to hemorrhage. Stronger-than-normal pulses occur in a healthy person during exercise. Explain the causes for the changes in the pulse under these conditions.

Capillary Exchange

There are about 10 billion capillaries in the body. Nutrients diffuse across the capillary walls into the interstitial spaces, and waste products diffuse in the opposite direction. In addition, a small amount of fluid is forced out of the capillaries into the interstitial space at their arterial ends. Most of that fluid, but not all, reenters the capillaries at their venous ends.

The major forces responsible for moving fluid through the capillary wall are (1) blood pressure and (2) osmosis (figure 13.20). Blood pressure forces fluid *out of* the capillary, and osmosis moves fluid *into* the capillary. Fluid moves

by osmosis from the interstitial space into the capillary because blood has a greater osmotic pressure than does interstitial fluid. Recall from chapter 3 that water moves to areas of higher concentration of dissolved molecules, and the greater the concentration of dissolved molecules in a fluid, the greater the osmotic pressure of the fluid. Blood has a greater osmotic pressure because of the large concentration of plasma proteins (see chapter 11) that are unable to cross the capillary wall. The concentration of proteins in the interstitial space is much lower than that in the blood. The capillary wall acts as a selectively permeable membrane, which prevents proteins from moving from the capillary into the interstitial space but allows fluid to move across the capillary wall.

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PROCESS Figure

PROCESS Figure 13.20 APR **Capillary Exchange**

Blood pressure and osmosis are the major forces responsible for movement of fluid across the capillary wall.

How would a high-sodium diet affect capillary exchange?

The exchange of materials across the capillary wall varies as blood passes from one end of the capillary to the other. Figure 13.20 highlights the effects

of blood pressure and osmosis on capillary exchange.

❶ At the arterial end of the capillary, the movement of fluid out of the capillary due to blood pressure is greater than the movement of fluid into the capillary due to osmosis. Consequently, there is a net movement of fluid out of the capillary into the interstitial space.

❷ Remember that resistance to blood flow is high in capillaries, and as blood flows though capillaries, blood pressure decreases rapidly. This results in lower blood pressure at the venous end of the capillary compared to the arterial end. Consequently, at the venous end of the capillary, the movement of fluid out of the capillary due to blood pressure is less than the movement of fluid into the capillary due to osmosis. Therefore, at the venous end of the capillary there is a net movement of fluid from the interstitial space into the capillary.

❸ Approximately nine-tenths of the fluid that leaves the capillary at the arterial end reenters the capillary at its venous end. The remaining one-tenth of the fluid enters lymphatic capillaries and is eventually returned to the general circulation (see chapter 14).

Edema, or swelling, results from a disruption in the normal inwardly and outwardly directed pressures across the capillary walls. For example, inflammation increases the permeability of capillaries. Proteins, mainly albumin, leak out of the capillaries into the interstitial spaces. The proteins increase the osmotic pressure in the interstitial fluid. Consequently, fluid passes from the arterial end of capillaries into the interstitial spaces at a greater rate, and fluid passes from the interstitial spaces into the venous ends of capillaries at a slower rate. The lymphatic capillaries cannot carry all the fluid away. Thus, fluid accumulates in the interstitial spaces, resulting in edema.

Apply It 4

Explain edema (a) in response to a decrease in plasma protein concentration and (b) as a result of increased blood pressure within a capillary.

13.7 CONTROL OF BLOOD FLOW IN TISSUES

Learning Outcomes *After reading this section, you should be able to*

A. Explain how local control mechanisms regulate blood flow.
B. Explain how nervous mechanisms control blood flow.
C. Explain how hormonal mechanisms control blood flow.

Blood flow through the body tissues is highly controlled and matched closely to the metabolic needs of tissues. Mechanisms that control blood flow through tissues are classified as (1) local control or (2) nervous and hormonal control. Nervous and hormonal control involves several mechanisms that work together and with local control. Figure 13.21 outlines the major categories of blood flow control. Each mechanism is then discussed in further detail.

Brain
Brainstem
Spinal cord
Left common carotid
Aortic arch
Heart
Local Control
Precapillary sphincter
Nervous Control
Carotid sinus baroreceptors
Aortic arch baroreceptors
Baroreceptor reflex responds to changes in arterial blood pressure.
Hormonal Control
Multiple hormonal mechanisms respond to changes in blood composition and blood pressure.

Figure 13.21 **Blood Flow Control**

The flow of blood through the blood vessels is closely regulated to ensure adequate delivery of oxygen and nutrients to tissues, as well as removal of waste products. Mechanisms include local control, nervous control through the baroreceptor and chemoreceptor reflexes, and various hormonal controls.

Local Control of Blood Flow

Local control of blood flow is achieved by the periodic relaxation and contraction of the precapillary sphincters. When the precapillary sphincters relax, blood flow through the capillaries increases. When the precapillary sphincters contract, blood flow through the capillaries decreases. The precapillary sphincters are controlled by the metabolic activity and needs of the tissues. Metabolism generates by-products, such as CO_2. The accumulation of CO_2 also leads to a decrease in pH. As these changes occur, blood flow increases, allowing for faster removal of these substances. During exercise, the metabolic activity of skeletal muscle increases dramatically, and the by-products of metabolism are produced more rapidly. The precapillary sphincters relax, increasing blood flow through the capillaries. Other factors that control blood flow through the capillaries are the tissue concentrations of O_2 and nutrients, such as glucose, amino acids, and fatty acids (table 13.1).

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TABLE 13.1 Homeostasis: Control of Blood Flow*

Stimulus	Response
Regulation by Metabolic Needs of Tissues	
Increased CO_2 and decreased pH or decreased O_2 and nutrients, such as glucose, amino acids, and fatty acids, due to increased metabolism	Relaxation of precapillary sphincters and subsequent increase in blood flow through capillaries
Decreased CO_2 and increased pH or increased O_2 and nutrients, such as glucose, amino acids, and fatty acids	Contraction of precapillary sphincters and subsequent decrease in blood flow through capillaries
Regulation by Nervous Mechanisms	
Increased physical activity or increased sympathetic activity	Constriction of blood vessels in skin and viscera
Increased body temperature detected by neurons of hypothalamus	Dilation of blood vessels in skin (see chapter 5)
Decreased body temperature detected by neurons of hypothalamus	Constriction of blood vessels in skin (see chapter 5)
Decrease in skin temperature below a critical value	Dilation of blood vessels in skin (protects skin from extreme cold)
Anger or embarrassment	Dilation of blood vessels in skin of face and upper thorax
Regulation by Hormonal Mechanisms (Reinforces Increased Activity of Sympathetic Division)	
Increased physical activity and increased sympathetic activity, causing release of epinephrine and small amounts of norepinephrine from adrenal medulla	Constriction of blood vessels in skin and viscera; dilation of blood vessels in skeletal and cardiac muscle
Long-Term Local Blood Flow	
Increased metabolic activity of tissues over a long period, as occurs in athletes who train regularly	Increased number of capillaries
Decreased metabolic activity of tissues over a long period, as occurs during periods of reduced physical activity	Decreased number of capillaries
*The mechanisms operate when the systemic blood pressure is maintained within a normal range of values.	

Figure 13.22 illustrates the local control of blood flow through tissues under different levels of activity.

PROCESS Figure

PROCESS Figure 13.22 **Local Control of Blood Flow Through Capillary Beds**

Precapillary sphincters relax and contract to regulate blood flow to tissues to match the tissues' needs.

Understand **Which condition (relaxation or contraction of precapillary sphincters) would most likely exist in your skeletal muscle tissue when you are sleeping? Explain your answer.**

❶ Blood flow through tissue increases as precapillary sphincters relax. Relaxation is stimulated by decreased concentrations of O_2 and nutrients, such as glucose, amino acids, and fatty acids, in the tissue. Increased levels of CO_2 and subsequent decrease in pH also lead to relaxation of the precapillary sphincters.

❷ Blood flow through tissue decreases as precapillary sphincters contract. Contraction is stimulated by increased concentrations of O_2 and nutrients, such as glucose, amino acids, and fatty acids, in the tissue. Decreased levels of CO_2 and a subsequent increase in pH also lead to contraction of the precapillary sphincters.

Apply

Apply It 5

A student has been sitting for a short time with her legs crossed. After getting up to walk out of class, she notices a red blotch on the back of one of her legs. On the basis of what you know about local control of blood flow, explain why this happens.

In addition to the control of blood flow through existing capillaries, if the metabolic activity of a tissue increases often, additional capillaries gradually grow into the area. The additional capillaries allow local blood flow to increase to a level that matches the longer-term metabolic needs of the tissue. For example, the density of capillaries in the well-trained skeletal muscles of athletes is greater than that in skeletal muscles on a typical nonathlete (table 13.1).

Nervous and Hormonal Control of Blood Flow

Nervous control of blood flow is carried out primarily through the sympathetic division of the autonomic nervous system. Sympathetic nerve fibers innervate most blood vessels of the body, except the capillaries and precapillary sphincters, which have no nerve supply.

An area of the lower pons and upper medulla oblongata, called the **vasomotor** (vay-soh-MOH-tor) **center,** continually transmits a low frequency of action potentials to the sympathetic nerve fibers that innervate blood vessels of the body. As a consequence, the peripheral blood vessels are continually in a partially constricted state, a condition called **vasomotor tone.** Changes in vasomotor tone alter blood flow as well as blood pressure. An increase in vasomotor tone causes blood vessels to constrict further and blood pressure to rise. A decrease in vasomotor tone causes blood vessels to dilate and blood pressure to fall. Nervous control of blood vessel diameter is an important way that blood pressure is regulated.

Nervous control of blood vessels also causes blood to be shunted from one large area of the body to another. For example, nervous control of blood vessels during exercise increases vasomotor tone in the viscera and skin and reduces vasomotor tone in exercising skeletal muscles. As a result, blood flow to the viscera and skin decreases, and blood flow to skeletal muscle increases.

It is important to note that the different mechanisms regulating blood flow work together to meet tissue needs. Nervous control of blood vessels during exercise and local control through the relaxation of precapillary sphincters together increase blood flow through exercising skeletal muscle several-fold (table 13.1).

The sympathetic division also regulates hormonal control of blood flow through the release of epinephrine and norepinephrine from the adrenal medulla. These hormones are transported in the blood to all parts of the body. In most blood vessels, these hormones cause constriction, which reduces blood flow. But in some tissues, such as skeletal muscle and cardiac muscle, these hormones cause the blood vessels to dilate, increasing blood flow.

Apply It 6

Raynaud syndrome is a treatable condition in which blood vessels, primarily in the fingers and toes, undergo exaggerated vasoconstriction in response to emotions or exposure to cold. Describe the effects on the fingers and toes of a person who has severe, untreated Raynaud syndrome. Explain why these consequences occur.

13.8 REGULATION OF ARTERIAL PRESSURE

Learning Outcomes *After reading this section, you should be able to*

A. Describe the short-term mechanisms that regulate arterial pressure.
B. Describe the long-term mechanisms that regulate arterial pressure.

Adequate blood pressure is required to maintain blood flow through the blood vessels of the body, and several regulatory mechanisms ensure that blood pressure remains adequate for this task. The **mean arterial blood pressure (MAP)** is slightly less than the average of the systolic and diastolic pressures in the aorta because diastole lasts longer than systole. The mean arterial pressure changes over our lifetime. MAP is about 70 mm Hg at birth, is maintained at about 95 mm Hg from adolescence to middle age, and may reach 110 mm Hg in a healthy older person.

The body's MAP is equal to the **cardiac output (CO)** times the **peripheral resistance (PR),** which is the resistance to blood flow in all the blood vessels:

$$\mathrm{MAP} = \mathrm{CO} \times \mathrm{PR}$$

Because the cardiac output is equal to the **heart rate (HR)** times the **stroke volume (SV),** the mean arterial pressure is equal to the heart rate times the stroke volume times the peripheral resistance (PR):

$$\mathrm{MAP} = \mathrm{HR} \times \mathrm{SV} \times \mathrm{PR}$$

Thus, the MAP increases in response to greater HR, SV, or PR, and the MAP decreases in response to lower HR, SV, or PR. The MAP is controlled on a minute-to-minute basis by changes in these variables. For example, when blood pressure suddenly drops because of hemorrhage or some other cause, control systems attempt to reestablish blood pressure by increasing HR, SV, and PR, so that blood pressure is maintained at a value consistent with life. Mechanisms are also activated to increase the blood volume to its normal

value. Mechanisms that regulate MAP include (1) baroreceptor reflexes, (2) chemoreceptor reflexes, and (3) hormonal mechanisms.

Baroreceptor Reflexes

Baroreceptor reflexes function to keep the blood pressure within its normal range. Figure 13.23 illustrates the communication among the various components of the baroreceptor reflex mechanism.

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PROCESS Figure

PROCESS Figure 13.23 APR **Baroreceptor Reflex Mechanisms**

The baroreceptor reflex helps control blood pressure.

A vasovagal response is when a person feels light-headed or even faints in response to a particular trigger, such as pain. It is due to a reduction in heart rate and drop in blood pressure. Which step in the above diagram is likely the most important to a vasovagal response? Explain your choice.

1. **Baroreceptors** respond to stretch in arteries caused by increased blood pressure. They are scattered along the walls of most of the large arteries of the neck and thorax, and many are located in the carotid sinus at the base of the internal carotid artery and in the walls of the aortic arch.
2. Action potentials travel along sensory nerve fibers from the baroreceptors to the cardioregulatory and vasomotor centers in the medulla oblongata.
3. The heart is innervated by the parasympathetic division of the autonomic nervous system (via the vagus nerve), which can decrease heart rate.
4. The heart is also innervated by the sympathetic division of the autonomic nervous system, which can increase heart rate and stroke volume.
5. The sympathetic division also innervates blood vessels, altering the degree of vasomotor tone and therefore peripheral resistance.

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As stated earlier, the baroreceptor reflexes respond to changes in blood pressure. The effects of the baroreceptor reflexes in response to an increase as well as a decrease in blood pressure are detailed next.

A sudden rise in blood pressure stretches the artery walls and greater action potential frequency in the baroreceptors. The greater action potential frequency delivered to the vasomotor and cardioregulatory centers in the medulla oblongata causes responses that lower the blood pressure. One major response is a decrease in vasomotor tone, resulting in dilation of blood vessels and decreased peripheral resistance. Other responses, controlled by the cardioregulatory center, are an increase in the parasympathetic stimulation of the heart, which decreases the heart rate, and a decrease in the sympathetic stimulation of the heart, which reduces the stroke volume. The decreased heart rate, stroke volume, and peripheral resistance lower the blood pressure toward its normal value (figure 13.24).

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Homeostasis Figure 13.24 **Baroreceptor Effects on Blood Pressure**

(1) Blood pressure is within its normal range. (2) Blood pressure increases outside the normal range, which causes homeostasis to be disturbed. (3) Baroreceptors detect the increase in blood pressure. The blood pressure control centers in the brain respond to changes in blood pressure. (4) Neural and hormonal changes alter the activity of cardiac muscle of the heart and the smooth muscle of the blood vessels (effectors), causing heart rate and stroke

volume to decrease and blood vessels to dilate. (5) These changes cause blood pressure to decrease. (6) Blood pressure returns to its normal range, and homeostasis is restored.

A sudden decrease in blood pressure results in a reduced action potential frequency in the baroreceptors. The lower frequency of action potentials delivered to the vasomotor and cardioregulatory centers in the medulla oblongata produces responses that raise blood pressure. Sympathetic stimulation of the heart increases, which increases the heart rate and stroke volume. In addition, vasomotor tone increases, resulting in constriction of blood vessels and greater peripheral resistance. The higher heart rate, stroke volume, and peripheral resistance raise the blood pressure toward its normal value (figure 13.24).

These **baroreceptor reflexes** regulate blood pressure on a moment-to-moment basis. When a person rises rapidly from a sitting or lying position, blood pressure in the neck and thoracic regions drops dramatically due to the pull of gravity on the blood. This reduction in blood pressure can be so great that it reduces blood flow to the brain enough to cause dizziness or even loss of consciousness. The falling blood pressure activates the baroreceptor reflexes, which reestablish normal blood pressure within a few seconds. A healthy person usually experiences only a temporary sensation of dizziness.

Chemoreceptor Reflexes

Chemoreceptor reflexes respond to changes in blood concentrations of O_2 and CO_2, as well as pH. Figure 13.25 illustrates the components of the chemoreceptor reflex.

PROCESS Figure

PROCESS Figure 13.25 **Chemoreceptor Reflex Mechanisms**

The chemoreceptor reflex helps control blood pressure.

How would holding your breath affect blood pressure?

CLINICAL IMPACT

Circulatory shock

Circulatory shock is inadequate blood flow throughout the body that causes tissue damage due to lack of O_2. Severe shock may damage vital body tissues and lead to death.

In mild cases of shock, the baroreceptor reflexes can be adequate to compensate for blood loss until the blood volume is restored. In more severe cases of shock, all of the regulatory mechanisms are needed to sustain life. But in the most severe cases, the regulatory mechanisms are not adequate to compensate for the effects of shock. As a consequence, a positive-feedback cycle begins to develop: The blood pressure regulatory mechanisms lose their ability to control the blood pressure, and shock worsens. As shock becomes worse, the effectiveness of the regulatory mechanisms

deteriorates even further. The positive-feedback cycle proceeds until death occurs or until treatment, such as a transfusion, terminates the cycle. Five types of shock are classified based on their cause:

1. **Hypovolemic shock** is the result of reduced blood volume. **Hemorrhagic shock,** caused by internal or external bleeding, is one type of hypovolemic shock. **Plasma loss shock** results from loss of plasma, as may occur in severely burned areas of the body. **Interstitial fluid loss shock** is reduced blood volume resulting from the loss of interstitial fluid, as may occur as a result of diarrhea, vomiting, or dehydration.

2. **Neurogenic shock** is caused by vasodilation in response to emotional upset or anesthesia.

3. **Anaphylactic shock** is caused by an allergic response that results in the release of inflammatory substances that cause vasodilation and increased capillary permeability. Large amounts of fluid then move from capillaries into the interstitial spaces.

4. **Septic shock** is caused by infections that release toxic substances into the circulatory system (*blood poisoning*), depressing the heart's activity and leading to vasodilation and increased capillary permeability.

5. **Cardiogenic shock** results from a decrease in cardiac output caused by events that decrease the heart's ability to function. Heart attack (myocardial infarction) is a common cause of cardiogenic shock. Fibrillation of the heart, which can be initiated by stimuli such as cardiac arrhythmias or exposure to electrical shocks, also results in cardiogenic shock.

❶ **Carotid bodies** are small structures that lie near the carotid sinuses, and **aortic bodies** lie near the aortic arch. These structures contain sensory receptors that respond to changes in blood O_2 concentration, CO_2 concentration, and pH. Because they are sensitive to chemical changes in the blood, they are called **chemoreceptors.** They send action potentials along sensory nerve fibers to the medulla oblongata.

❷ There are also chemoreceptors in the medulla oblongata, which monitor blood CO_2 and pH.

❸ When O_2 or pH levels decrease or when CO_2 levels increase, the chemoreceptors respond with an increased frequency of action potentials and activate the **chemoreceptor reflexes.** In response, the vasomotor and cardiovascular centers decrease parasympathetic stimulation of the heart, which increases the heart rate.

❹ The cardioregulatory centers also increase sympathetic stimulation of the heart, which further increases heart rate, stroke volume.

❺ The vasomotor center also increase sympathetic stimulation of blood vessels, which increases vasoconstriction.

All these changes result in increased blood pressure. This increased blood pressure causes a greater rate of blood flow to the lungs, which helps raise blood O_2 levels and reduce blood CO_2 levels. The chemoreceptor reflexes function under emergency conditions and usually do not play an important role in regulating the cardiovascular system. They respond strongly only when the O_2 levels in the blood fall to very low levels or when CO_2 levels become substantially elevated.

Hormonal Mechanisms

In addition to the rapidly acting baroreceptor and chemoreceptor reflexes, four important hormonal mechanisms help control blood pressure. These include (1) the adrenal medullary mechanisms, (2) the renin-angiotensin-aldosterone mechanism, (3) the antidiuretic mechanism, and (4) the atrial natriuretic mechanism.

Adrenal Medullary Mechanism

Figure 13.26 illustrates the adrenal medullary mechanism.

PROCESS Figure

PROCESS Figure 13.26 Hormonal Regulation: Adrenal Medullary Mechanism

Stimuli that increase sympathetic stimulation of the heart and blood vessels also increase sympathetic stimulation of the adrenal medulla and lead to secretion of epinephrine and some norepinephrine.

What would happen to a person's blood pressure if they were injected with epinephrine—for instance, in response to anaphylactic shock?

❶ Stimuli that lead to increased sympathetic stimulation of the heart and blood vessels also cause increased stimulation of the adrenal medulla.

❷ The adrenal medulla responds by releasing epinephrine and small amounts of norepinephrine into the blood.

❸ Epinephrine binds to receptors on the heart and increases heart rate and stroke volume.

❹ Additionally, epinephrine binds to receptors on blood vessels and causes vasoconstriction, especially of blood vessels in the skin and viscera.

These changes lead to an increase in blood pressure. Epinephrine also causes vasodilation of blood vessels in skeletal muscle and cardiac muscle, thereby increasing the supply of blood flowing to those muscles and preparing the body for physical activity.

Renin-Angiotensin-Aldosterone Mechanism

The renin-angiotensin-aldosterone mechanism is important when there is a drop in blood pressure. Three different substances are involved in this complex mechanism: (1) renin, (2) angiotensin II, and (3) aldosterone. In addition, other substances are important in the production of angiotensin II. Figure 13.27 illustrates the renin-angiotensin-aldosterone mechanism.

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PROCESS Figure

PROCESS Figure 13.27 Hormonal Regulation: Renin-Angiotensin-Aldosterone Mechanism

The kidneys detect decreased blood pressure and respond by increasing renin secretion. The results are vasoconstriction, increased water reabsorption, and

decreased urine formation; changes that return blood pressure to homeostatic levels.

Why does increased Na^+ reabsorption cause increased water reabsorption at the kidneys?

1. The kidneys detect a decrease in blood pressure and respond by secreting an enzyme called **renin** (REE-nin) into the circulatory system.
2. Renin travels through the blood and acts on the plasma protein **angiotensinogen** (an-jee-oh-TEN-sin-oh-jen) to produce **angiotensin I** (an-jee-oh-TEN-sin).
3. Another enzyme, called **angiotensin-converting enzyme (ACE),** found in large amounts in organs, such as the lungs, acts on angiotensin I to convert it to its active form, **angiotensin II.**
4. Angiotensin II is a potent vasoconstrictor, which causes blood pressure to increase. Thus, in response to reduced blood pressure, the kidneys' release of renin increases the blood pressure toward its normal value.
5. Angiotensin II also acts on the adrenal cortex to increase the secretion of **aldosterone** (al-DOS-ter-ohn).
6. Aldosterone acts on the kidneys, causing them to conserve Na^+ and water. As a result, the volume of water lost from the blood into the urine is reduced. The decrease in urine volume results in less fluid loss from the body, which maintains blood volume. Adequate blood volume is essential to maintain normal venous return to the heart and thereby maintain blood pressure (see chapter 12).

Antidiuretic Hormone Mechanism

When the concentration of solutes in the plasma increases or when blood pressure decreases substantially, nerve cells in the hypothalamus respond by causing the release of **antidiuretic** (an-tee-die-you-RET-ik; to decrease urine production) **hormone (ADH)**, also called *vasopressin* (vay-soh-PRESS-in; to cause vasoconstriction), from the posterior pituitary gland (figure 13.28). ADH acts on the kidneys and causes them to absorb more water, thereby decreasing urine volume. This response helps maintain blood volume and blood pressure. The release of large amounts of ADH causes vasoconstriction of blood vessels, which causes blood pressure to increase.

Figure 13.28 **Hormonal Regulation: Antidiuretic Hormone Mechanism**

Increases in the osmolality of blood or decreases in blood pressure result in antidiuretic hormone (ADH) secretion. ADH increases water reabsorption by the kidneys, and large amounts of ADH result in vasoconstriction. These changes maintain blood pressure.

Atrial Natriuretic Mechanism

A peptide hormone called **atrial natriuretic** (ay-TREE-al nay-tree-yoo-RET-ik) **hormone** is released primarily from specialized cells of the right atrium in response to elevated blood pressure. Atrial natriuretic hormone causes the kidneys to promote the loss of Na^+ and water in the urine, increasing urine volume. Loss of water in the urine causes blood volume to decrease, thus decreasing the blood pressure.

Summary of Regulatory Mechanisms

Blood pressure regulation involves both short-term and long-term mechanisms. Baroreceptor mechanisms are most important in controlling blood pressure on a short-term basis (see figures 13.23 and 13.24). They are sensitive to sudden changes in blood pressure, and they respond quickly. The chemoreceptor and adrenal medullary reflexes are also sensitive to sudden changes in blood pressure and respond quickly, but they respond to large changes in blood pressure. The renin-angiotensin-aldosterone, antidiuretic hormone, and atrial natriuretic mechanisms are more important in maintaining blood pressure on a long-term basis. They are influenced by small changes in blood pressure or concentration and respond by gradually bringing the blood pressure back into its normal range (figure 13.29).

Homeostasis Figure 13.29 **Long-Term Control of Blood Pressure**

(1) Blood pressure is within its normal range. (2) Blood pressure increases outside the normal range, which causes homeostasis to be disturbed. (3) Increased blood pressure is detected by cardiac muscle cells and the kidneys (receptors). The heart and kidneys (control center) respond to increased blood pressure by the secretions of hormones. (4) Blood vessels of the body and the kidneys (effectors) respond to the hormones by dilating or adjusting

blood volume through urine formation. (5) These changes cause blood pressure to decrease. (6) Blood pressure returns to its normal range, and homeostasis is restored.

Apply It 7

Suppose that a hemorrhage results in rapid loss of a large volume of blood. What blood pressure regulation mechanisms will come into play? If the hemorrhage results in the loss of the same volume of blood over a period of several hours, will the same mechanisms respond? Explain.

The walls of all arteries undergo changes as people age. Some arteries change more rapidly than others, and some individuals are more susceptible to change than others. The most significant effects of aging occur in the large, elastic arteries, such as the aorta; in large arteries carrying blood to the brain; and in the coronary arteries.

Changes in arteries that make them less elastic, referred to as arteriosclerosis, occur in nearly every individual and become more severe with advancing age. A type of arteriosclerosis called **atherosclerosis** (ATH-er-oh-skler-OH-sis) results from the deposition of material in the walls of arteries that forms plaques. The material is composed of a fatlike substance containing cholesterol. The fatty material can eventually be dominated by the deposition of dense connective tissue and calcium salts.

Several factors influence the development of atherosclerosis. Lack of exercise, smoking, obesity, and a diet high in cholesterol and fats appear to increase the severity of atherosclerosis and the rate at which it develops. Severe atherosclerosis is more prevalent in some families than in others, which suggests a genetic influence. Some evidence suggests that a low-fat diet, mild exercise, and relaxation activities slow the progression of atherosclerosis and may even reverse it to some degree.

Atherosclerosis greatly increases resistance to blood flow because the deposits narrow the inside diameter of the arteries. The added resistance hampers normal circulation to tissues and greatly increases the work the heart must perform. Furthermore, the rough atherosclerotic plaques attract platelets, which adhere to them and increase the chance of thrombus formation.

Capillaries narrow and become more irregular in shape with age. Their walls become thicker, and consequently the efficiency of capillary exchange decreases.

Veins tend to develop patchy thickenings in their walls, resulting in narrowing in these areas. The tendency to develop varicose veins increases with age (see Clinical Impact, "Varicose Veins" earlier in this chapter), as does the tendency to develop hemorrhoids (varicose veins of the rectum or anus) because some veins increase in diameter due to weakening of the connective tissue in their walls. There is a related increase in the development of thromboses and emboli, especially in veins that are dilated or those in which blood flow is sluggish.

SUMMARY

13.1 Functions of the Circulatory System

The circulatory system can be divided into the pulmonary vessels and the systemic vessels. The circulatory system and the heart maintain sufficient blood flow to tissues. The circulatory system carries blood; exchanges nutrients, waste products, and gases; transports hormones; regulates blood pressure; and directs blood flow.

13.2 General Features of Blood Vessel Structure

1. The heart pumps blood through elastic arteries, muscular arteries, and arterioles to the capillaries.
2. Blood returns to the heart from the capillaries through venules, small veins, medium-sized veins, and large veins.
3. Except for capillaries and venules, blood vessels have three layers:
   a. The tunica intima, the innermost layer, consists of endothelium, a basement membrane, and connective tissue.
   b. The tunica media, the middle layer, contains circular smooth muscle and elastic fibers.
   c. The outer tunica adventitia is composed of connective tissue.

Arteries

1. Large, elastic arteries have many elastic fibers but little smooth muscle in their walls. They carry blood from the heart to smaller arteries with little decrease in pressure.
2. The walls of muscular arteries have much smooth muscle and some elastic fibers. They undergo vasodilation and vasoconstriction to control blood flow to different regions of the body.
3. Arterioles, the smallest arteries, have smooth muscle cells and a few elastic fibers. They undergo vasodilation and vasoconstriction to control blood flow to local areas.

Capillaries

1. Capillaries consist of only endothelium and are surrounded by a basement membrane and loose connective tissue.
2. Nutrient and waste exchange is the principal function of capillaries.
3. Blood is supplied to capillaries by arterioles. Precapillary sphincters regulate blood flow through capillary networks.

Veins

1. Venules are composed of endothelium surrounded by a basement membrane.
2. Small veins are venules covered with a layer of smooth muscle and a layer of connective tissue.
3. Medium-sized and large veins contain less smooth muscle and fewer elastic fibers than arteries of the same size.
4. Valves prevent the backflow of blood in the veins.

13.3 Blood Vessels of the Pulmonary Circulation

The pulmonary circulation moves blood to and from the lungs. The pulmonary trunk carries oxygen-poor blood from the heart to the lungs, and pulmonary veins carry oxygen-rich blood from the lungs to the left atrium of the heart.

13.4 Blood Vessels of the Systemic Circulation: Arteries

Aorta

The aorta leaves the left ventricle to form the ascending aorta, the aortic arch, and the descending aorta, which consists of the thoracic aorta and the abdominal aorta.

Arteries of the Head and Neck

1. The brachiocephalic, left common carotid, and left subclavian arteries branch from the aortic arch to supply the head and the upper limbs.
2. The common carotid arteries and the vertebral arteries supply the head. The common carotid arteries divide to form the external carotids (which supply the face and mouth) and the internal carotids (which supply the brain).

Arteries of the Upper Limbs

The subclavian artery continues as the axillary artery and then as the brachial artery, which branches to form the radial and ulnar arteries.

Thoracic Aorta and Its Branches

The thoracic aorta has visceral branches, which supply the thoracic organs, and parietal branches, which supply the thoracic wall.

Abdominal Aorta and Its Branches

The abdominal aorta has visceral branches, which supply the abdominal organs, and parietal branches, which supply the abdominal wall.

Arteries of the Pelvis

Branches of the internal iliac arteries supply the pelvis.

Arteries of the Lower Limbs

The common iliac arteries give rise to the external iliac arteries, and the external iliac artery continues as the femoral artery and then as the popliteal artery in the leg. The popliteal artery divides to form the anterior and posterior tibial arteries.

13.5 Blood Vessels of the Systemic Circulation: Veins

The superior vena cava drains the head, neck, thorax, and upper limbs. The inferior vena cava drains the abdomen, pelvis, and lower limbs.

Veins of the Head and Neck

1. The internal jugular veins drain the brain, anterior head, and anterior neck.

2. The external jugular veins drain the posterior head and posterior neck.

Veins of the Upper Limbs

The deep veins are the brachial, axillary, and subclavian; the superficial veins are the cephalic, basilic, and median cubital.

Veins of the Thorax

The left and right brachiocephalic veins and the azygos veins return blood to the superior vena cava.

Veins of the Abdomen and Pelvis

1. Posterior abdominal wall veins join the azygos veins.
2. Veins from the kidneys, adrenal glands, and gonads directly enter the inferior vena cava.
3. Veins from the stomach, intestines, spleen, and pancreas connect with the hepatic portal vein, which transports blood to the liver for processing. The hepatic veins from the liver join the inferior vena cava.

Veins of the Lower Limbs

1. The deep veins course with the deep arteries and have similar names.
2. The superficial veins are the great and small saphenous veins.

13.6 Physiology of Circulation

Blood Pressure

1. Blood pressure is a measure of the force exerted by blood against the blood vessel walls.
2. Blood pressure moves blood through vessels.
3. Blood pressure can be measured by listening for Korotkoff sounds produced as blood flows through arteries partially constricted by a blood pressure cuff.

Pressure and Resistance

In a normal adult, blood pressure fluctuates between 120 mm Hg (systolic) and 80 mm Hg (diastolic) in the aorta. If blood vessels constrict, resistance to blood flow increases, and blood flow decreases.

Pulse Pressure

1. Pulse pressure is the difference between systolic and diastolic pressures. Pulse pressure increases when stroke volume increases.
2. A pulse can be detected when large arteries are near the body surface.

Capillary Exchange

1. Most exchange across the wall of the capillary occurs by diffusion.
2. Blood pressure, capillary permeability, and osmosis affect movement of fluid across the wall of the capillaries. There is a net movement of fluid from the blood into the tissues. The fluid gained by the tissues is removed by the lymphatic system.

13.7 Control of Blood Flow in Tissues

Local Control of Blood Flow

Blood flow through a tissue is usually proportional to the metabolic needs of the tissue and is controlled by the precapillary sphincters.

Nervous and Hormonal Control of Blood Flow

1. The vasomotor center (sympathetic division) controls blood vessel diameter. Other brain areas can excite or inhibit the vasomotor center.
2. Vasomotor tone is the state of partial constriction of blood vessels.
3. The nervous system is responsible for routing the flow of blood, except in the capillaries, and for maintaining blood pressure.
4. Epinephrine and norepinephrine released by the adrenal medulla alter blood vessel diameter.

13.8 Regulation of Arterial Pressure

Mean arterial pressure (MAP) is proportional to cardiac output times the peripheral resistance.

Baroreceptor Reflexes

1. Baroreceptors are sensitive to stretch.
2. Baroreceptors are located in the carotid sinuses and the aortic arch.
3. The baroreceptor reflex changes peripheral resistance, heart rate, and stroke volume in response to changes in blood pressure.

Chemoreceptor Reflexes

1. Chemoreceptors are sensitive to changes in blood O_2, CO_2, and pH.
2. Chemoreceptors are located in the carotid bodies and the aortic bodies.
3. The chemoreceptor reflex increases peripheral resistance in response to low O_2 levels, high CO_2 levels, and reduced blood pH.

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Hormonal Mechanisms

1. Epinephrine released from the adrenal medulla as a result of sympathetic stimulation increases heart rate, stroke volume, and vasoconstriction.
2. The kidneys release renin in response to low blood pressure. Renin promotes the production of angiotensin II, which causes vasoconstriction and increased secretion of aldosterone. Aldosterone reduces urine output.
3. ADH released from the posterior pituitary causes vasoconstriction and reduces urine output.
4. The heart releases atrial natriuretic hormone when atrial blood pressure increases. Atrial natriuretic hormone stimulates an increase in urine production, causing a decrease in blood volume and blood pressure.

Summary of Regulatory Mechanisms

1. The baroreceptor, chemoreceptor, and adrenal medullary reflex mechanisms are most important in short-term regulation of blood pressure.
2. Hormonal mechanisms, such as the renin-angiotensin-aldosterone system, antidiuretic hormone, and atrial natriuretic hormone, are more important in long-term regulation of blood pressure.

REMEMBERING AND UNDERSTANDING

1. Name, in order, all the types of blood vessels, starting at the heart, going to the tissues, and returning to the heart.
2. Name the three layers of a blood vessel. What kinds of tissue are in each layer?
3. Relate the structures of the different types of arteries to their functions.
4. Describe a capillary network. Name the structure that regulates blood flow through the capillary network.
5. Describe the structure of capillaries, and explain their major function.
6. Describe the structure of veins.
7. What is the function of valves in blood vessels, and which blood vessels have valves?
8. List the parts of the aorta. Name the major arteries that branch from the aorta and deliver blood to the vessels that supply the heart, the head and upper limbs, and the lower limbs.
9. Name the arteries that supply the major areas of the head, upper limbs, thorax, abdomen, and lower limbs. Describe the area each artery supplies.
10. Name the major vessels that return blood to the heart. What area of the body does each drain?
11. List the veins that drain blood from the thorax, abdomen, and pelvis. What specific area of the body does each drain? Describe the hepatic portal system.
12. List the major veins that drain the upper and lower limbs.
13. Define blood pressure, and describe how it is normally measured.
14. Describe the changes in blood pressure, starting in the aorta, moving through the vascular system, and returning to the right atrium.
15. Define pulse pressure, and explain what information can be determined by monitoring the pulse.
16. Explain how blood pressure and osmosis affect the movement of fluid between capillaries and tissues. What happens to excess fluid that enters the tissues?
17. Explain what is meant by local control of blood flow through tissues, and describe what carries out local control.
18. Describe nervous control of blood vessels. Define vasomotor tone.
19. Define mean arterial pressure. How is it related to heart rate, stroke volume, and peripheral resistance?

20. Where are baroreceptors located? Describe the baroreceptor reflex when blood pressure increases and when it decreases.
21. Where are the chemoreceptors for CO_2 and pH located? Describe what happens when O_2 levels in the blood decrease.
22. For each of the following hormones—epinephrine, renin, angiotensin II, aldosterone, ADH, and atrial natriuretic hormone—state where each is produced, what stimulus causes increased hormone production, and the hormone's effect on the circulatory system.

CRITICAL THINKING

1. For each of the following destinations, name all the arteries a red blood cell encounters if it starts its journey in the left ventricle:
   a. brain
   b. external part of the skull
   c. left hand
   d. anterior portion of the right leg
2. For each of the following starting places, name all the veins a red blood cell encounters on its way back to the right atrium:
   a. left side of the brain
   b. external part of the right side of the skull
   c. left hand
   d. medial portion of the right leg
   e. kidney
   f. small intestine
3. In angioplasty, a surgeon threads a catheter through blood vessels to a blocked coronary artery. The tip of the catheter can expand, stretching the coronary artery and unblocking it, or the tip of the catheter can be equipped with tiny blades capable of removing the blockage. Typically, the catheter is first inserted into a large blood vessel in the superior, medial part of the thigh. Starting with this blood vessel, name all the blood vessels the catheter passes through to reach the anterior interventricular artery.

4. A 55-year-old male has a colonoscopy that reveals a large tumor in his colon. His doctor orders a liver scan to determine if the cancer has spread from the colon to the liver. Based on your knowledge of blood vessels, explain how cancer cells from the colon can end up in the liver.

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5. High blood pressure can be caused by advanced atherosclerosis of the renal arteries, even though blood flow appears sufficient to allow a normal volume of urine to be produced. Explain how atherosclerosis of the renal arteries can result in high blood pressure.
6. Preston ran a race during which his stroke volume and heart rate increased. Vasoconstriction occurred in his viscera, and his blood pressure rose, but not dramatically. Explain these changes in his circulatory system.
7. Nitroglycerin is often given to people who experience angina pains. This drug causes vasodilation of arteries and veins, which reduces the amount of work the heart performs and increases blood flow through the coronary arteries. Explain why dilation of arteries and veins reduces the heart's amount of work.

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

14

Lymphatic System and Immunity

The lymphatic system is important to the defense of the body, but it also plays are role in maintaining the fluid balance as well as in the absorption of lipids in the digestive tract.

LEARN TO APPLY IT

Ouch! Shay was not happy about this trip to see his pediatrician. He would be starting kindergarten soon and his mother had warned him it was time for his "booster" shots. He had not known what

was in store, but he never thought it would be this. Just before administering the vaccine, the nurse reassured him that the pain was well worth the benefit. But as a 5-year-old, Shay wasn't so sure. Some vaccination procedures require a "booster" shot, another dose of the original vaccine given some time after the original dose.

Explain why it was beneficial for Shay to receive his booster shot before starting school.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 10 Lymphatic System

14.1 FUNCTIONS OF THE LYMPHATIC SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Describe the functions of the lymphatic system.
B. Explain how lymph is formed.

One of the basic tenets of life is that many organisms consume or use other organisms in order to survive. Some microorganisms, such as certain bacteria or viruses, use humans as a source of nutrients and as an environment where they can survive and reproduce. As a result, some of these microorganisms can damage the body, causing disease or even death. Microorganisms that cause disease or damage to the tissues of the body are considered **pathogens.** In addition, foreign substances, such as toxins, may harm the body as well. Not surprisingly, the body has ways to resist or destroy these threats. This chapter considers how the lymphatic system and the components of other systems, such as white blood cells and phagocytes, continually provide protection to the body.

The **lymphatic** (lim-FAT-ik) **system** is important for the protection of the body, but in addition to that, this system carries out other functions. The functions of the lymphatic system include:

1. *Maintenance of fluid balance.* About 30 liters (L) of fluid pass from the blood capillaries into the interstitial spaces each day, whereas only 27 L pass from the interstitial spaces back into the blood capillaries (see chapter 13). If the extra 3 L of interstitial fluid remained in the interstitial spaces, edema would result, causing tissue damage and eventually death. Instead, the 3 L of fluid enters the lymphatic capillaries. Once inside the lymphatic capillaries, this fluid is called **lymph** (LIMF) and it passes through the lymphatic vessels to return to the blood. In addition to water, lymph contains solutes derived from two sources: (a) Substances in plasma, such as ions, nutrients, gases, and some proteins, pass from blood capillaries into the interstitial spaces, and then into lymphatic capillaries to become part of the lymph; (b) substances such as hormones,

enzymes, and waste products, derived from cells within the tissues, are also part of the lymph.

2. *Lipid absorption.* The lymphatic system absorbs lipids and other substances from the digestive tract (see figure 16.15) through lymphatic vessels called **lacteals** (LAK-tee-als) located in the lining of the small intestine. Lipids enter the lacteals and pass through the lymphatic vessels to the venous circulation. The lymph passing through these lymphatic vessels appears white because of its lipid content and is called **chyle** (KILE).
3. *Defense.* Pathogens, such as microorganisms and other foreign substances, are filtered from lymph by lymph nodes and from blood by the spleen. In addition, lymphocytes and other cells are capable of destroying pathogens. Because the lymphatic system is involved with fighting infections, as well as filtering blood and lymph to remove pathogens, many infectious diseases produce symptoms associated with the lymphatic system (see table 14.3).

14.2 ANATOMY OF THE LYMPHATIC SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Describe how lymph is transported.
B. Describe the structure and function of tonsils, lymph nodes, the spleen, and the thymus.

Lymphatic Capillaries and Vessels

The lymphatic system includes (1) lymph, (2) lymphatic vessels, (3) lymph nodes, (4) the tonsils, (5) the spleen, and (6) the thymus (figure 14.1*a*). The lymphatic system, unlike the circulatory system, does not circulate fluid to and from tissues. Instead, the lymphatic system carries fluid in one direction, from tissues to the circulatory system. Fluid moves from blood capillaries into tissue spaces (see figure 13.20). Most of the fluid returns to the blood, but some of the fluid moves from the tissue spaces into lymphatic capillaries to become lymph (figure 14.2*a*). The **lymphatic capillaries** are tiny, closed-ended vessels consisting of simple squamous epithelium. The lymphatic capillaries are more permeable than blood capillaries because they lack a basement membrane, and fluid moves easily into them. Overlapping squamous cells of the lymphatic capillary walls act as valves that prevent the backflow of fluid (figure 14.2*b*). After fluid enters lymphatic capillaries, it flows through them towards vessels in the thoracic cavity.

Figure 14.1 **Lymphatic System and Lymph Drainage**

(*a*) The major lymphatic organs are the tonsils, the lymph nodes, the spleen, and the thymus. Lymph nodes are located along lymphatic vessels throughout the body, but aggregations of them are found in the cervical, axillary, and inguinal areas. (*b*) Lymph from the lighter areas flows into the thoracic duct before entering the blood. Lymph from the darkened area flows into the right lymphatic duct before entering the blood.

Figure 14.2 **Lymph Formation and Movement**

(*a*) Fluid moves from blood capillaries into tissues and from tissues into lymphatic capillaries to form lymph. (*b*) The overlap of epithelial cells of the lymphatic capillary allows fluid to enter easily but prevents it from moving back into the tissue. Valves, located farther along in lymphatic vessels, also ensure one-way flow of lymph.

Lymphatic capillaries are present in most tissues of the body. Exceptions are the central nervous system, bone marrow, and tissues lacking blood vessels, such as the epidermis and cartilage. A superficial group of lymphatic capillaries collects excess interstitial fluids from the dermis and subcutaneous tissue, and a deep group collects excess fluid from muscle, the viscera, and other deep structures.

Similar to blood capillaries, lymphatic capillaries join to form larger **lymphatic vessels,** which resemble small veins (figure 14.2*b*). Small lymphatic vessels have a beaded appearance because they have one-way valves that are similar to the valves of

veins (see figure 13.4). When a lymphatic vessel is compressed, the valves prevent backward movement of lymph. Consequently, compression of the lymphatic vessels causes lymph to move forward through them. Three factors cause compression of the lymphatic vessels: (1) contraction of surrounding skeletal muscle during activity, (2) periodic contraction of smooth muscle in the lymphatic vessel wall, and (3) pressure changes in the thorax during breathing.

The lymphatic vessels converge and eventually empty into the blood at two locations in the body. (1) Lymphatic vessels from the right upper limb and the right half of the head, neck, and chest form the **right lymphatic duct,** which empties into the right subclavian vein. (2) Lymphatic vessels from the rest of the body enter the **thoracic duct,** which empties into the left subclavian vein. Figure 14.1*b* indicates the pattern of lymph flow from different areas of the body.

Lymphatic Organs

The **lymphatic organs** include (1) the tonsils, (2) the lymph nodes, (3) the spleen, and (4) the thymus. **Lymphatic tissue** is characterized by housing many lymphocytes and other defense cells, such as macrophages. Lymphatic tissue is found within lymphatic organs as well as other organs. The lymphocytes originate from red bone marrow (see chapter 11) and are carried by the blood to lymphatic organs. Lymphatic tissue has very fine reticular fibers (see chapter 4). These fibers form an interlaced network that holds the lymphocytes and other cells in place. When lymph or blood filters through lymphatic organs, the fiber network also traps pathogens and other items in the fluid. Lymphocytes within lymphatic tissue respond to the pathogens by dividing and increasing in number. The increased number of lymphocytes is part of the immune response that causes the destruction of pathogens.

Tonsils

There are three groups of **tonsils** (figure 14.3; see figure 15.2): (1) the paired palatine tonsils, (2) the pharyngeal tonsils, and (3) the lingual tonsil. The **palatine** (PAL-ah-tine; palate) **tonsils** are located on each side of the posterior opening of the oral cavity; these are the ones usually referred to as “the tonsils.” The **pharyngeal** (fah-RIN-jee-al) **tonsil** is located near the internal opening of the nasal cavity. When the pharyngeal tonsil is enlarged, it is commonly called the **adenoid** (ADD-eh-noyd), or adenoids. An enlarged pharyngeal tonsil can interfere with normal breathing. The **lingual** (LING-gwal; tongue) **tonsil** is on the posterior surface of the tongue.

Figure 14.3 APR

Anterior view of the oral cavity, showing the tonsils. Part of the palate is removed (*dotted line*) to show the pharyngeal tonsil.

The tonsils form a protective ring of lymphatic tissue around the openings between the nasal and oral cavities and the pharynx. They protect against pathogens and other potentially harmful material entering from the nose and mouth. Sometimes the palatine or pharyngeal tonsils become chronically infected and must be removed. The removal of the palantine tonsils is called a **tonsillectomy**, and the removal of the pharyngeal tonsil is called an **adenoidectomy**. The lingual tonsil becomes infected less often than the other tonsils and is more difficult to remove. In adults, the tonsils decrease in size and may eventually disappear.

Lymph Nodes

Lymph nodes are rounded structures, varying from the size of a small seed to that of a shelled almond. Lymph nodes are distributed along the various lymphatic vessels (see figure 14.1*a*), and most lymph passes through at least one lymph node before entering the blood. Lymph nodes are found throughout the body and they are classified as superficial or deep. There are three superficial aggregations of lymph nodes on each side of the body: (1) inguinal nodes in the groin, (2) the axillary nodes in the axilla (armpit), and (3) the cervical nodes in the neck.

A dense connective tissue **capsule** surrounds each lymph node (figure 14.4). Extensions of the capsule, called **trabeculae,** subdivide a lymph node into compartments containing lymphatic tissue and lymphatic sinuses. The lymphatic tissue consists of lymphocytes and other cells that can form dense aggregations of tissue called **lymphatic nodules.** Note that lymphatic nodules are not the same as lymph nodes. Lymphatic nodules are areas of tissue within lymph nodes and other organs as well. **Lymphatic sinuses** are spaces between the lymphatic tissue that contain macrophages on a network of fibers.

Figure 14.4 APR **Lymph Node**

Arrows indicate direction of lymph flow. As lymph moves through the sinuses, phagocytic cells remove foreign substances. The germinal centers are sites of lymphocyte production.

Lymph flows through lymph nodes, passing through the different areas just described. Lymph enters the lymph node through afferent vessels. Once inside the lymph node, lymph passes through the lymphatic tissue and sinuses and eventually exits through efferent vessels.

As lymph moves through the lymph nodes, two functions are performed. One function is to activate the immune system. Pathogens in the lymph can stimulate lymphocytes in the lymphatic tissue to divide. The lymphatic nodules containing the rapidly dividing lymphocytes are called **germinal centers.** The newly produced lymphocytes are released into the lymph and eventually reach the blood, where they circulate and enter other lymphatic tissues. The lymphocytes are part of the adaptive immune response (see section 14.5, "Adaptive Immunity") that destroys pathogens. The second function of the lymph nodes is to remove pathogens from the lymph through the action of macrophages.

Apply It 1

Cancer cells can spread from a tumor site to other areas of the body through the lymphatic system. At first, however, as the cancer cells pass through the lymphatic system, they are trapped in the lymph nodes, which filter the lymph. During radical cancer surgery, malignant (cancerous) lymph nodes are removed, and their vessels are cut and tied off to prevent the cancer from spreading. Describe the consequences of tying off the lymphatic vessels.

The **spleen** (SPLEEN) is roughly the size of a clenched fist and is located in the left, superior corner of the abdominal cavity (figure 14.5). The spleen has an outer **capsule** of dense connective tissue and a small amount of smooth muscle. **Trabeculae** from

the capsule divide the spleen into small, interconnected compartments containing two specialized types of lymphatic tissue: (1) white pulp and (2) red pulp. **White pulp** is lymphatic tissue surrounding the arteries within the spleen. **Red pulp** is associated with the veins. It consists of a fibrous network, filled with macrophages and red blood cells, and enlarged capillaries that connect to the veins.

Figure 14.5 APR **Spleen**

(*a*) Inferior view of the spleen. (*b*) Section showing the arrangement of arteries, veins, white pulp, and red pulp. White pulp is associated with arteries, and red pulp is associated with veins.

The spleen filters blood instead of lymph. Cells within the spleen detect and respond to foreign substances in the blood and destroy old and damaged red blood cells. Lymphocytes in the white pulp can be stimulated in the same manner as in lymph nodes. Before blood leaves the spleen through veins, it passes through the red pulp. Macrophages in the red pulp remove foreign substances and worn-out red blood cells through phagocytosis.

The spleen also functions as a blood reservoir, holding a small volume of blood. In emergency situations, such as hemorrhage, smooth muscle in splenic blood vessels and in the splenic capsule can contract, allowing a small amount of blood to move out of the spleen into the general circulation.

Although it is protected by the ribs, the spleen is often ruptured in traumatic abdominal injuries. A ruptured spleen can cause severe bleeding, shock, and death. Surgical intervention may stop the bleeding. Cracks in the spleen are repaired using sutures and blood-clotting agents. Mesh wrapped around the spleen can hold it together. A **splenectomy** (splee-NEK-toh-mee), removal of the spleen, may be necessary if these techniques do not stop the bleeding. Other lymphatic organs and the liver then compensate for the loss of the spleen's functions.

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Thymus

The **thymus** (THIGH-mus) is a bilobed gland roughly triangular in shape (figure 14.6*a*). It is located in the superior mediastinum, the partition dividing the thoracic cavity into left and right parts. Each lobe of the thymus is surrounded by a thin connective tissue **capsule. Trabeculae** from the capsule divide each lobe into

lobules (figure 14.6*b*). Near the capsule and trabeculae, lymphocytes are numerous and form dark-staining areas called the **cortex.** A lighter-staining, central portion of the lobules, called the **medulla,** has fewer lymphocytes.

Figure 14.6 APR

(*a*) Location and shape of the thymus. (*b*) Histology of thymic lobules, showing the outer cortex and the inner medulla.

(b) ©Trent Stephens

The thymus is the site for the maturation of a class of lymphocytes called T cells (described in section 14.5, "Adaptive Immunity"). Large numbers of T cells are produced in the thymus, but most degenerate. The T cells that survive the maturation process are capable of reacting to pathogens. The mature T cells migrate to the medulla, enter the blood, and travel to other lymphatic tissues, where they help protect against pathogens. Production of T cells declines later in life due to decreased function of the thymus (see "Effects of Aging on the Lymphatic System and Immunity" later in this chapter).

Overview of the Lymphatic System

The lymphatic system plays important roles in the body to help maintain homeostasis, whether by regulating fluid balance or protecting the body against disease. Figure 14.7 summarizes the processes performed by the lymphatic system and how it interacts with other systems, such as the cardiovascular and digestive systems.

PROCESS Figure

PROCESS Figure 14.7 APR Overview of the Lymphatic System

The lymphatic system functions to help regulate fluid levels in the tissue and provide protection against pathogens.

Understand **The lymph nodes and spleen both function as filters. How do they differ in this filtration role?**

❶ Lymphatic capillaries and vessels remove fluid from tissues.

❷ Specialized lymphatic vessels called lacteals absorb lipids at the small intestine. The lymph in these vessels is referred to as chyle due to the high lipid content.

❸ Lymph nodes filter lymph removing pathogens and debris as the lymph flows toward the thoracic cavity.

❹ Lymph passes into larger vessels, such as the thoracic duct, and then enters the blood.

❺ The spleen filters blood and is a site where lymphocytes respond to infections.

❻ Pre-T cells are produced in red bone marrow and migrate to the thymus, where they mature to become T cells.

❼ B cells, which are produced and mature in the red bone marrow, and T cells from the thymus circulate to, and populate, other lymphatic tissues.

B cells and T cells are responsible for much of immunity. In response to infections, B cells and T cells increase in number and circulate to lymphatic tissue and other tissues. How B cells and T cells protect the body is discussed later in this chapter (see section 14.5, "Adaptive Immunity").

14.3 IMMUNITY

Learning Outcome *After reading this section, you should be able to*

A. Define the concepts of specificity and memory as they apply to immunity.

Immunity (im-YOU-nih-tee) is the ability to resist damage from pathogens, such as microorganisms; harmful chemicals, such as toxins released by microorganisms; and internal threats, such as cancer cells. Immunity is categorized into two systems that work together to protect the body: (1) **innate** (IH-nate, ih-NATE) **immunity** (also called *nonspecific resistance*) and (2) **adaptive immunity** (also called *specific immunity*). In innate immunity, the body recognizes and destroys certain pathogens, but the response to them is the same each time the body is exposed. In adaptive immunity, the body recognizes and destroys pathogens, but the response to them improves each time the pathogen is encountered. Adaptive immunity involves two subdivisions: (1) antibody-mediated immunity, which involves B cells, and (2) cell-mediated immunity, which involves specific T cells (figure 14.8). Although the immune system can be described in terms of these categories, these categories are artificial divisions used to emphasize particular aspects of immunity. In actuality, there is only one immune system, but its response often involves components of more than one type of immunity.

Innate Immunity

Physical barriers prevent entry
- Skin
- Mucous membranes
- Secretions (mucus, sweat, tears, etc.)

Chemical mediators act directly or indirectly to destroy pathogens
- Complement
- Histamine
- Leukotrienes
- Interferons

White blood cells fight against pathogens
- Phagocytic cells
- Cells of inflammations
- NK cells

Inflammatory responses often activate other aspects of immunity to protect the body.

Adaptive Immunity

Cell mediated immunity involves cytotoxic T lymphocytes directly destroying pathogens and diseased cells.

Antibody-mediated immunity involves B lymphocytes and the production of antibodies to fight against extracellular antigens.

Figure 14.8 **Components of Immunity**
The body is protected by many different lines of defense. We organize these into two major divisions: innate immunity and adaptive immunity.

Specificity and memory are characteristics of adaptive immunity, but not innate immunity. **Specificity** is the ability of adaptive immunity to recognize a particular substance. For example, innate immunity can act against bacteria in general, whereas adaptive immunity can distinguish among various kinds of bacteria. **Memory** is the ability of adaptive immunity to "remember" previous encounters with a particular substance. Essentially the body is "trained," and "better equipped" to deal with the pathogen. As a result, future responses are faster, stronger, and longer-lasting.

In innate immunity, specificity and memory are not involved. As a consequence, each time the body is exposed to a substance, the innate immune response is the same. For example, each time bacteria of a specific type are introduced into the body, phagocytosis proceeds with the same speed and efficiency to destroy those bacteria. In adaptive immunity, in contrast, the response during the second exposure to the same bacteria is faster and stronger than the response to the first exposure. Following the first exposure to the bacteria, the body can take many days to destroy them before the adaptive immunity mechanisms eliminate the bacteria. During this time, the bacteria damage tissues, producing the symptoms of disease. Following the second exposure to the same bacteria, the adaptive immunity response is rapid and effective. Bacteria are destroyed before any symptoms develop, and the person is said to be **immune**.

Though we describe the different components of immunity separately, understand that innate and adaptive immunity are intimately linked. Most important, mediators of innate immunity are required for the initiation and regulation of the adaptive response.

14.4 INNATE IMMUNITY

Learning Outcomes ***After reading this section, you should be able to***

A. Define innate immunity.
B. Describe the cells and chemical mediators involved in innate immunity.
C. List the events of an inflammatory response, and explain their significance.

Innate immunity involves many mechanisms that help protect the body. These mechanisms include (1) physical barriers, (2) chemical mediators, (3) white blood cells, and (4) the inflammatory response.

Physical Barriers

Physical barriers prevent pathogens and chemicals from entering the body in two ways: (1) The skin and mucous membranes form barriers that prevent their entry, and (2) tears, saliva, urine, and other secretions wash these substances from body surfaces. Pathogens cannot cause a disease if they cannot get into the body.

Chemical Mediators

Chemical mediators are molecules responsible for many aspects of innate immunity. Some chemicals on the surface of cells destroy pathogens or prevent their entry into the cells. For example, lysozyme in tears and saliva kills certain bacteria, and mucus on the mucous membranes prevents the entry of some pathogens. Other chemical mediators, such as histamine (HIS-tah-meen), complement, **prostaglandins** (PROS-tah-GLAN-dins), and **leukotrienes** (loo-koh-TRY-eens), promote inflammation by causing vasodilation and increasing vascular permeability. Some of these substances also enhance phagocytosis by certain white blood cells. In addition, interferons protect cells against viral infections.

Complement

Complement (KOM-pleh-ment) is a group of more than 20 proteins found in blood plasma. The operation of complement proteins is similar to that of clotting proteins (see chapter 11). Normally, complement proteins circulate in the blood in an inactive form. Certain complement proteins can be activated by combining with foreign substances, such as parts of a bacterial cell, or by combining with antibodies (see "Effects of Antibodies" in section 14.5). Once activation begins, a series of reactions results, in which each complement protein activates the next. Once activated, certain complement proteins promote inflammation and phagocytosis and can directly lyse (rupture) bacterial cells.

Interferons

Interferons (in-ter-FEER-ons) are proteins that protect the body against viral infections. When a virus infects a cell, the infected cell produces viral nucleic acids and proteins, which are assembled into new viruses. The new viruses are then released to infect other cells. Because infected cells usually stop their normal functions or die during viral replication, viral infections are clearly harmful to the body. Fortunately, viruses often stimulate infected cells to produce interferons, which do not protect the cell that produces them. Instead, interferons bind to the surface of neighboring cells, which then stimulate those cells to produce antiviral proteins. In this way interferon is like a "Save yourself!" signal from an infected cell to its neighbors. These antiviral proteins inhibit viral reproduction by preventing the production of new viral nucleic acids and proteins.

Some interferons play a role in activating immune cells, such as macrophages and natural killer cells (see "White Blood Cells" in this section).

White Blood Cells

White blood cells (see chapter 11) and the cells derived from them are the most important cellular components of immunity. White blood cells are produced in red bone marrow and lymphatic tissue and released into the blood. Chemicals released from pathogens or damaged tissues attract the white blood cells, and they leave the blood and enter affected tissues. Important chemicals known to attract white blood cells include complement, leukotrienes, kinins (KYE-nins), and histamine. The movement of white blood cells toward these chemicals is called **chemotaxis** (kee-moh-TAK-sis).

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CLINICAL IMPACT

Treating Viral Infections and Cancer with Interferons

Because viruses induce some cancers, interferons may play a role in controlling cancers. Interferons activate macrophages and natural killer cells (a type of lymphocyte), which attack tumor cells. Through genetic engineering, interferons currently are produced in sufficient quantities for clinical use and, along with other therapies, have been effective in treating certain viral infections and cancers. For example, interferons are used to treat hepatitis C, a viral disorder that can cause cirrhosis and cancer of the liver, and to treat genital warts caused by the herpes virus. Interferons are also approved for the treatment of Kaposi sarcoma, a cancer that can develop in AIDS patients.

Phagocytic Cells

Phagocytosis (FAG-oh-sigh-TOH-sis) is the ingestion and destruction of particles by cells called **phagocytes** (FAG-oh-sites) (see chapter 3). The particles can be microorganisms or their parts, foreign substances, or dead cells from the body. The most important phagocytes are neutrophils and macrophages, although other white blood cells also have limited phagocytic ability.

Neutrophils (NEW-troh-fills) are small phagocytic white blood cells. Neutrophils are usually the first white blood cells to enter infected tissues from the blood in large numbers. They release chemical signals that increase the inflammatory response by recruiting and activating other immune cells. Neutrophils often die after phagocytizing a single microorganism. **Pus** is an accumulation of fluid, dead neutrophils, and other cells at a site of infection.

Macrophages (MAK-roh-fay-jes) are monocytes that leave the blood, enter tissues, and enlarge about fivefold. Monocytes and macrophages form the **mononuclear phagocytic system** because they are phagocytes with a single (mono), unlobed nucleus. Sometimes macrophages are given specific names, such as *dust cells* in the lungs, *Kupffer cells* in the liver, and *microglia* in the central nervous system.

Macrophages can ingest more and larger items than can neutrophils. Macrophages usually appear in infected tissues after neutrophils, and they are responsible for most of the phagocytic activity in the late stages of an infection, including cleaning up dead neutrophils and other cellular debris.

In addition to leaving the blood in response to an infection, macrophages are also found in uninfected tissues. If pathogens enter uninfected tissue, the macrophages may phagocytize the pathogens before they can replicate or cause damage. For example, macrophages are located at potential points where pathogens may enter the body, such as beneath the skin and mucous membranes, and around blood and lymphatic vessels. They also remove materials from lymph as it passes through lymph nodes and blood as it flows through the spleen and liver.

Cells of Inflammation

Basophils, which are derived from red bone marrow, are motile white blood cells that can leave the blood and enter infected tissues. **Mast cells,** which are also derived from red bone marrow, are nonmotile cells in connective tissue, especially near capillaries. Like macrophages, mast cells are located at points where pathogens may enter the body, such as the skin, lungs, gastrointestinal tract, and urogenital tract.

Basophils and mast cells can be activated through innate immunity (e.g., by complement) or through adaptive immunity (see section 14.5, "Adaptive Immunity"). When activated, these cells release chemicals, such as histamine and leukotrienes, that produce an inflammatory response or activate other mechanisms, such as smooth muscle contraction in the lungs. **Eosinophils** also participate in inflammation associated with allergies and asthma.

Inflammation is beneficial in the fight against pathogens, but too much inflammation can be harmful, destroying healthy tissues as well as the microorganisms.

Natural Killer Cells

Natural killer (NK) cells are a type of lymphocyte produced in red bone marrow, and they account for up to 15% of lymphocytes. NK cells recognize classes of cells, such as tumor cells or virus-infected cells, in general, rather than specific tumor cells or cells infected by a specific virus. For this reason, and because NK cells do not exhibit a memory response, they are classified as part of innate immunity. NK cells use a variety of methods to destroy their target cells, including releasing chemicals that damage cell membranes and cause the cells to lyse.

Inflammatory Response

The **inflammatory response** to injury involves many of the chemicals and cells previously discussed. Most inflammatory responses are very similar, although some details vary, depending on the intensity of the response and the type of injury. In figure 14.9, we use a bacterial infection to illustrate an inflammatory response. Bacteria enter the tissue, causing damage that stimulates the release or activation of chemical mediators, such as histamine, prostaglandins, leukotrienes, complement, and kinins. These chemicals produce several effects: (1) Vasodilation increases blood flow

and brings phagocytes and other white blood cells to the area; (2) phagocytes leave the blood and enter the tissue; and (3) increased vascular permeability allows fibrinogen and complement to enter the tissue from the blood. Fibrinogen is converted to fibrin (see chapter 11), which isolates the infection by walling off the infected area. Complement further enhances the inflammatory response and attracts additional phagocytes. This process of releasing chemical mediators and attracting phagocytes and other white blood cells continues until the bacteria are destroyed. Phagocytes remove microorganisms and dead tissue, and the damaged tissues are repaired.

Figure 14.9 **Inflammatory Response**

Bacteria cause tissue damage and the release of chemical mediators that initiate inflammation and phagocytosis, resulting in the destruction of the bacteria. If any bacteria remain, additional chemical mediators are activated. After all the bacteria are destroyed, the tissue is repaired.

Inflammation can be local or systemic. **Local inflammation** is an inflammatory response confined to a specific area of the body. Symptoms of local inflammation include redness, heat, and swelling due to increased blood flow and increased vascular permeability, as well as pain caused by swelling and by chemical mediators acting on pain receptors. The tissue destruction, swelling, and pain lead to loss of function (see chapter 4).

Systemic inflammation is an inflammatory response that is generally distributed throughout the body. In addition to the local symptoms at the sites of inflammation, three additional features can be present:

1. Red bone marrow produces and releases large numbers of neutrophils, which promote phagocytosis.
2. **Pyrogens** (PYE-roh-jens; fever-producing), chemicals released by microorganisms, neutrophils, and other cells, stimulate fever production. Pyrogens affect the body's temperature-regulating mechanism in the hypothalamus in the brain. As a consequence, heat production and conservation increase, raising body temperature. Fever is beneficial because it promotes the activities of the immune system, such as phagocytosis, and inhibits the growth of some microorganisms.
3. In severe cases of systemic inflammation, vascular permeability can increase so much that large amounts of fluid are lost from the blood into the tissues. The decreased blood volume can cause shock and death (see Clinical Impact, "Circulatory Shock" in chapter 13).

14.5 ADAPTIVE IMMUNITY

Learning Outcomes *After reading this section, you should be able to*

A. Define antigen.
B. Describe the origin, development, activation, and proliferation of lymphocytes.
C. Define antibody-mediated immunity and name the cells responsible.
D. Define cell-mediated immunity, and name the cells responsible.
E. Diagram the structure of an antibody.
F. Describe the effects produced by antibodies.
G. Discuss the primary and secondary responses to an antigen.
H. Explain the basis for long-lasting immunity.

Adaptive immunity exhibits two defining characteristics: (1) specificity and (2) memory. As explained earlier in this chapter, specificity is the ability to recognize a particular substance, and memory is the ability to respond with increasing

effectiveness to successive exposures to the antigen. **Antigens** (AN-tih-jens; *anti* (body) + *-gen,* producing) are substances that stimulate adaptive immune responses. Antigens can be divided into two groups: (1) foreign antigens and (2) self-antigens.

Foreign antigens are introduced from outside the body. Microorganisms, such as bacteria and viruses, and chemicals released by microorganisms are examples of foreign antigens. Pollen, animal hairs, foods, and drugs can cause an **allergic reaction** because they are foreign antigens that produce an overreaction of the immune system (see table 14.3). Tissue and organ transplants are often used to treat certain diseases; however, transplanted tissues and organs contain foreign antigens, and the response to these antigens can cause rejection of the transplant.

MICROBES IN YOUR BODY

Do Our Gut Bacteria Drive Immune Development and Function?

Over the last four decades, there have been increasing numbers of people suffering from allergies and autoimmune disorders. Researchers hypothesize that the increase in these conditions stems from inadequate development of immune function. In turn, they hypothesize that underdeveloped immune function is due to deficiencies in our gut microbiota. This has led to the Hygiene Hypothesis, which states that increased use of antibiotics and antimicrobial chemicals damages normal gut and other microbiota critical for immune system development and function.

The importance of the gut in immune development is supported by the fact that it contains the largest concentration of lymphatic tissue and microbiota in the human body. In humans, the gut microbiota begin to appear just before birth, and as the baby passes through the birth canal, more microorganisms are transferred from the mother to the baby. At about 10 years of age, a person's gut microbiota is established and remains similar throughout life. Humans and their gut microbiota have a symbiotic relationship in that the gut provides space and nutrients for the microbiota which, in turn, provide their host with specialized nutrition, physiological regulators, and protection against pathogens. Because of these ever-present microbiota ("good" bacteria), human gut epithelial and immune cells must maintain tolerance to them but still protect against invading gut pathogens ("bad" bacteria).

How do our cells distinguish between "good" and "bad" bacteria? As it turns out, gut microbiota help stimulate development of immune cells by triggering production of different receptors. These receptors are found in cell membranes of white blood cells such as macrophages, neutrophils, and also in cell membranes of intestinal epithelial cells. The surface of all bacterial cells has bacteria-specific molecules that can be recognized by the receptors of defense cells and is what allows for distinction between "good" and "bad" microorganisms. Without appropriate amounts and/or types of gut microbiota, the body's immune system may not have all of the essential messages for production of specific immune cells and chemicals that kill pathogenic intestinal microorganisms.

Medical professionals are interested in manipulating gut microbiota to reduce allergies and other diseases, and to promote healing. First, and perhaps most importantly, is to get the desired population of gut microbiota started immediately through breastfeeding. Human breast milk contains certain carbohydrates that stimulate growth of specific intestinal microbiota but also prevent infection by some pathogens. If problems should arise later in life, the use of prebiotics (non-digestible carbohydrates that promote the growth of healthy microbiota) and probiotics (live normal gut microbiota) is being actively explored. However, there is still much work to be done

before we fully understand the extent to which gut microbiota are involved in human immune function.

Self-antigens are molecules produced by body cells to identify them as "self" or part of the body. Some of these self-antigens also provide important information about the health of the cell. Some self-antigens are used by defense cells to determine if a cell is mutated or infected. This is beneficial. For example, the recognition of tumor antigens can result in destruction of the tumor. But the response to self-antigens can also be harmful. **Autoimmune disease** results when self-antigens stimulate unwanted destruction of normal tissue. An example is rheumatoid arthritis, which destroys the tissue within joints.

Adaptive immunity can be divided into antibody-mediated immunity and cell-mediated immunity. **Antibody-mediated immunity** involves a group of lymphocytes called **B cells** and proteins called **antibodies** (AN-tee-bod-ees), which are found in the plasma. Antibodies are produced by **plasma cells,** which are derived from the B cells. **Cell-mediated immunity** involves the actions of a second type of lymphocyte, called **T cells.** Several subpopulations of T cells exist. For example, **cytotoxic** (sigh-toh-TOK-sik; destructive to cells) **T cells** produce the effects of cell-mediated immunity, and **helper T cells** can promote or inhibit the activities of both antibody-mediated immunity and cell-mediated immunity.

Table 14.1 summarizes and contrasts the main features of innate immunity and the two categories of adaptive immunity (i.e., (1) antibody-mediated immunity and (2) cell-mediated immunity).

Table 14.1 Comparison of Innate and Adaptive Immunity

Primary Cells	Origin of Cells	Site of Maturation	Location of Mature Cells	Primary Secretory Product	Primary Actions
Innate Immunity					
Neutrophils, eosinophils, basophils, mast cells, monocytes, and macrophages	Red bone marrow	Red bone marrow (neutrophils, eosinophils, basophils, and monocytes) and tissues (mast cells and macrophages)	Blood, connective tissue, and lymphatic tissue	Histamine, complement, prostaglandins, leukotrienes, kinins, and interferons	Inflammatory response and phagocytosis
Adaptive Immunity					
Antibody-mediated immunity (B cells)	Red bone marrow	Red bone marrow	Blood and lymphatic tissue	Antibodies	Protection against extracellular antigens (bacteria, toxins, and viruses outside of cells)

Primary Cells	Origin of Cells	Site of Maturation	Location of Mature Cells	Primary Secretory Product	Primary Actions
Cell-mediated immunity (T cells)	Red bone marrow	Thymus	Blood and lymphatic tissue	Cytokines	Protection against intra-cellular antigens (viruses and intracellular bacteria) and tumors; responsible for graft rejection

Origin and Development of Lymphocytes

To understand how lymphocytes are responsible for antibody-mediated and cell-mediated immunity, it is important to know how lymphocytes originate and become specialized immune cells. **Hemopoietic stem cells** in red bone marrow are capable of giving rise to all the blood cells (see figure 11.2). Some stem cells give rise to pre-T cells, which migrate through the blood to the thymus, where they divide and are processed into T cells (figure 14.10). Other stem cells produce pre-B cells, which are processed in the red bone marrow into B cells.

Figure 14.10 **Origin and Processing of B Cells and T Cells**

Both B cells and T cells originate from stem cells in red bone marrow. B cells are processed from pre-B cells in the red bone marrow, whereas T cells are processed from pre-T cells in the thymus. Both B cells and T cells circulate to other lymphatic tissues, such as lymph nodes.

After processing, B cells enter the blood from red bone marrow, and T cells enter the blood from the thymus. Both types of cells move through the blood to lymphatic tissues (see figure 14.7). These lymphocytes live for a few months to many years and continually circulate between the blood and the lymphatic tissues. Normally, there are

about five times as many T cells as B cells in the blood. When stimulated by an antigen, B cells and T cells divide, producing cells that are responsible for the destruction of antigens.

Small groups of identical B cells or T cells, called **clones,** form during embryonic development. Each clone is derived from a single, unique B cell or T cell. Each clone can respond only to a particular antigen. However, there is such a large variety of clones that the immune system can react to most antigens. Among the antigens to which the clones can respond are normal self-antigens. Because this response could destroy the body's own cells, clones acting against normal self-antigens are usually eliminated or suppressed. Most of this process occurs during prenatal development, but it also continues after birth and throughout a person's lifetime.

Activation and Multiplication of Lymphocytes

The specialized B-cell or T-cell clones can respond to antigens and produce an adaptive immune response. For the adaptive immune response to be effective, two events must occur: (1) antigen recognition by lymphocytes and (2) proliferation of the lymphocytes recognizing the antigen.

Antigen Recognition

Lymphocytes have cell membrane proteins, called **antigen receptors,** on their surfaces. The antigen receptors on B cells are called **B-cell receptors,** and those on T cells are called **T-cell receptors.** Each receptor binds with only a specific antigen. Each clone consists of lymphocytes that have identical antigen receptors on their surfaces. Activation of the lymphocytes of a particular clone occurs when antigens combine with the antigen receptors of a clone. Once lymphocytes are activated, the adaptive immune response begins.

In many cases, the antigens that activate lymphocytes are actually a portion of larger molecules. B cells and T cells typically recognize antigens after these large molecules have been processed or broken down into smaller fragments. These large molecules can originate from either (1) internal antigens or (2) external antigens. Internal antigens are substances produced in a cell that are then processed for display to a lymphocyte. These may include normal cell products or substances resulting from infection, as in the case of a virus. External antigens are foreign antigens that are phagocytized by macrophages or other phagocytic cells. These phagocytic cells are referred to as antigen-presenting cells. In both cases, processed antigen fragments are bound to major histocompatibility complex molecules, transported to the cell membrane, and presented to specific lymphocytes.

Major histocompatibility complex (MHC) molecules are glycoproteins that have binding sites for antigens. Different MHC molecules have different binding sites —that is, they are specific for certain antigens. It is important not to confuse the MHC molecules with the antigen receptors described above. Though both types of receptors interact with antigens, MHC molecules are a different group of receptors found on the membrane of many types of cells. There are two classes of MHC molecules: (1) MHC

class I molecules and (2) MHC class II molecules. MHC class I molecules are found on the membranes of most nucleated cells, and display internal antigens. MHC class II molecules are found on the membranes of antigen-presenting cells, and display external antigens. Antigen-presenting cells include macrophages, B lymphocytes, and other defense cells. The MHC molecules function as "serving trays" that hold and present a processed antigen on the outer surface of the cell membrane. The combined MHC molecule and processed antigen can then bind to a lymphocyte's antigen receptor and stimulate it. Figure 14.11, illustrates how helper T cells are stimulated when combined with MHC class II molecules.

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PROCESS Figure

PROCESS Figure 14.11 APR **Proliferation of Helper T Cells**

An antigen-presenting cell (macrophage) stimulates helper T cells to divide.

Cellular communication is an important aspect of immunity. In this figure, paracrine communication and autocrine communication are both shown. In which step is paracrine communication taking place? In which step is autocrine communication taking place? (See table 10.1 for descriptions of cellular communication.)

❶ An antigen-presenting cell, such as a macrophage, phagocytizes, processes, and displays an antigen on its cell membrane on a MHC class II molecule.

❷ A helper T cell interacts with the macrophage through its T-cell receptor.

❸ Costimulation (described in more detail below) occurs through other chemical signaling, such as interleukins secreted by the macrophage and CD4 glycoproteins of the helper T cell.

❹ The helper T cell is activated and stimulated to divide through the actions of interleukin-2 (described below), producing daughter cells.

❺ The newly formed "daughter" helper T cells can be stimulated to divide as well. These helper T cells can also stimulate B cells and cytotoxic T cells.

❻ Some daughter cells will become memory T cells. Memory helper T cells become active in future encounters with the same antigen.

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The MHC molecule/antigen combination is usually only the first signal necessary to produce a response from a B cell or T cell. In many cases, **costimulation** by a second signal is also required. Costimulation can be achieved by **cytokines** (SIGH-toh-kines), which are proteins or peptides secreted by one cell as a regulator of neighboring cells. For example, **interleukin-1** (in-ter-LOO-kin)is a cytokine released by macrophages that can stimulate helper T cells (figure 14.11, step 3).

Lymphocytes have other surface molecules besides MHC molecules that help bind cells together and stimulate a response. For example, helper T cells have a glycoprotein called CD4, which helps connect helper T cells to the macrophage by binding to MHC class II molecules. The CD4 protein is also bound by the virus that causes AIDS (see table 14.3). As a result, the virus preferentially infects helper T cells. Cytotoxic T cells have a glycoprotein called CD8, which helps connect cytotoxic T cells to cells displaying MHC class I molecules.

Lymphocyte Proliferation

Lymphocyte proliferation is an important process that generates the needed defense cells to protect the body. Increases in T cells and B cells are important, but the processes differ for each lymphocyte class. We will first focus on the proliferation of helper T cells. Before exposure to a particular antigen, the number of helper T cells that can respond to that antigen is too small to produce an effective response against it. After the antigen is processed and presented to a helper T cell by a macrophage, the

helper T cell responds by producing **interleukin-2** and **interleukin-2 receptors** (figure 14.11, step 4). Interleukin-2 binds to the receptors and stimulates the helper T cell to divide. The "daughter" helper T cells produced by this division can again be presented with the antigen by macrophages and again be stimulated to divide. Thus, the number of helper T cells is greatly increased.

It is important for the number of helper T cells to increase because helper T cells are necessary for the activation of most B cells or cytotoxic T cells. For example, B cells have receptors that can recognize antigens. Most B cells, however, do not respond to antigens without stimulation from helper T cells. Without functional helper T cells, the immune response of B cells would not be effective to prevent disease.

Recall that B cells act as antigen presenting cells. Figure 14.11 focused on the activation of a helper T cell and its proliferation. Figure 14.12 focuses on the proliferation of B cells after interacting with a helper T cell.

PROCESS Figure

PROCESS Figure 14.12 **Proliferation of B Cells**

A helper T cell stimulates a B cell to divide and differentiate into plasma cells, which produce antibodies.

Considering that antibodies are proteins that will be released from the cell, which types of cytoplasmic organelles are likely to be found in high numbers in plasma cells. (See table 3.1 for a summary of organelles and their functions.)

❶ B-cell proliferation begins when a B cell takes in the same kind of antigen that stimulated the helper T cell.

❷ The antigen is processed by the B cell and presented on the B-cell surface by an MHC class II molecule.

❸ A helper T cell is stimulated when it binds to the MHC class II/antigen complex. There is also costimulation involving CD4 and interleukins.

❹ As a result, the B cell divides into two "daughter" cells.

❺ One of these daughter cells differentiates into a **plasma cell,** which produces antibodies.

❻ The division process continues, increasing the number of cells capable of producing antibodies and resulting in sufficient antibodies to destroy all the antigen.

❼ Daughter cells that do not become plasma cells, reduce in size and become memory B cells. Memory B cells become active in future encounters with the same antigen.

Apply It 2

How does elimination of the antigen stop the production of antibodies?

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Antibody-Mediated Immunity

Exposure of the body to an antigen can lead to the activation of B cells and the production of antibodies. The antibodies bind to the antigens, which can be destroyed through several different mechanisms. Because antibodies are in body fluids, antibody-mediated immunity is effective against extracellular antigens, such as bacteria, viruses (when they are outside cells), and toxins. Antibody-mediated immunity is also involved in certain allergic reactions.

Structure of Antibodies

Antibodies are proteins produced in response to an antigen. They are Y-shaped molecules consisting of four polypeptide chains: two identical heavy chains and two identical light chains (figure 14.13). The end of each "arm" of the antibody is the **variable region.** This region is the part of the antibody that combines with the antigen. The variable region of a particular antibody can join only with a particular antigen; this is similar to the lock-and-key model of enzymes (see chapter 2). The rest of the antibody is the **constant region,** and it has several functions. For example, the

constant region can activate complement, or it can attach the antibody to cells, such as macrophages, basophils, and mast cells.

Figure 14.13 **Structure of an Antibody**

The Y-shaped antibody has two "arms." Each arm has a variable region that functions as an antigen-binding site. The constant region can activate complement or bind to other immune system cells, such as macrophages, basophils, or mast cells.

Antibodies make up a large portion of the proteins in plasma. Most plasma proteins can be separated into albumin and alpha, beta, and gamma globulin portions (see chapter 11). Antibodies are sometimes called **gamma globulins** (GAM-ah GLOB-you-lins), because they are found mostly in the gamma globulin part of plasma. Antibodies are also called **immunoglobulins (Ig)** because they are globulin proteins involved in immunity. The five general classes of antibodies are denoted IgG, IgM, IgA, IgE, and IgD (table 14.2).

TABLE 14.2 Classes of Antibodies and Their Functions

Antibody	Total Serum Antibody (%)	Description	Structure

Antibody	Total Serum Antibody (%)	Description	Structure
IgG	80–85	Activates complement and increases phagocytosis; can cross the placenta and provide immune protection to the fetus and newborn; responsible for Rh reactions, such as hemolytic disease of the newborn	
IgM	5–10	Activates complement and acts as an antigen-binding receptor on the surface of B cells; responsible for transfusion reactions in the ABO blood system; often the first antibody produced in response to an antigen	
IgA	15	Secreted into saliva, into tears, and onto mucous membranes to protect body surfaces; found in colostrum and milk to provide immune protection to the newborn	

Antibody	Total Serum Antibody (%)	Description	Structure
IgE	0.002	Binds to mast cells and basophils and stimulates the inflammatory response	
IgD	0.2	Functions as an antigen-binding receptor on B cells	

Effects of Antibodies

Antibodies can affect antigens either directly or indirectly. Direct effects occur when a single antibody binds to an antigen and inactivates the antigen, or when many antigens are bound together and are inactivated by many antibodies (figure 14.14*a,b*). The ability of antibodies to join antigens together is the basis for many clinical tests, such as blood typing, because when enough antigens are bound together, they form visible clumps (see figure 11.15).

Figure 14.14 **Effects of Antibodies**

Antibodies directly affect antigens by inactivating the antigens or by binding the antigens together. Antibodies indirectly affect antigens by activating other mechanisms through the constant region of the antibody. Indirect mechanisms include activation of complement, increased inflammation resulting from the release of inflammatory chemicals from mast cells or basophils, and increased phagocytosis resulting from antibody attachment to macrophages.

Most of the effectiveness of antibodies results from indirect effects (figure 14.14*c*–*e*). After an antibody has attached by its variable region to an antigen, the constant region of the antibody can activate other mechanisms that destroy the antigen. For example, the constant region of antibodies can activate complement, which stimulates inflammation, attracts white blood cells through chemotaxis, and lyses bacteria. When an antigen combines with the antibody, the constant region triggers the release of inflammatory chemicals from mast cells and basophils. For example, people who have hay fever inhale the antigens (usually plant pollens), which are then absorbed through

the respiratory mucous membrane. The combination of the antigen with antibodies stimulates mast cells to release inflammatory chemicals, such as histamine. The resulting localized inflammatory response produces swelling and excess mucus production in the respiratory tract. Finally, macrophages can attach to the constant region of the antibody and phagocytize both the antibody and the antigen.

Antibody Production

The production of antibodies after the first exposure to an antigen is different from that following a second or subsequent exposure. Figure 14.15 illustrates the difference in a primary response and a secondary response to the same antigen. Note the difference in the magnitude of the response and the relative number of cells produced.

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PROCESS Figure

PROCESS Figure 14.15 APR **Antibody Production**

Antibody production in a primary response has a longer response time and produces lower numbers of antibodies compared to a secondary response.

Understand **Which cell type is most important for the secondary response? Explain your answer.**

❶ The **primary response** results from the first exposure of a B cell to an antigen. When the antigen binds to the antigen-binding receptor on the B cell and the B cell has been activated by a helper T cell, the B cell undergoes several divisions to form plasma cells and memory B cells. Plasma cells produce antibodies. The primary response normally takes 3–14 days to produce enough antibodies to be effective against the antigen. In the meantime, the individual usually develops disease symptoms because the antigen has had time to cause tissue damage.

❷ **Memory B cells** are responsible for the **secondary response,** or *memory response*, which occurs when the immune system is exposed to an antigen against which it has already produced a primary response. When exposed to the antigen, the memory B cells quickly divide to form plasma cells, which rapidly produce antibodies. The secondary response provides better protection than the primary response for two reasons: (1) The time required to start producing antibodies is less (hours to a few days), and (2) more plasma cells and antibodies are produced. As a consequence, the antigen is quickly destroyed, no disease symptoms develop, and the person is immune.

The secondary response also includes the formation of new memory cells, which provide protection against additional exposures to a specific antigen. Memory cells are the basis of adaptive immunity. After destruction of the antigen, plasma cells die, the antibodies they released are degraded, and antibody levels decline to the point where they can no longer provide adequate protection. However, memory cells persist for many years—for life, in some cases. If memory cell production is not stimulated, or if the memory cells produced are short-lived, it is possible to have repeated infections of the same disease. For example, the same cold virus can cause the common cold more than once in the same person. This information may be useful for answering the Learn to Apply It question at the beginning of the chapter.

Apply It 3

One theory for long-lasting immunity assumes that humans are continually exposed to disease-causing agents. Explain how this exposure can produce lifelong immunity.

Cell-Mediated Immunity

Cell-mediated immunity is a function of cytotoxic T cells and is most effective against microorganisms that live inside body cells. Viruses and some bacteria are examples of intracellular microorganisms. Cell-mediated immunity is also involved with some allergic reactions, the control of tumors, and graft rejection.

Cell-mediated immunity is essential for fighting viral infections. When viruses infect cells, they direct the cells to make new viruses, which are then released to infect other cells. Thus, cells are turned into “virus factories.” While inside the cell, viruses have a safe haven from antibody-mediated immunity because antibodies cannot cross the cell membrane. Cell-mediated immunity fights viral infections by destroying virally infected cells. Figure 14.16 illustrates the proliferation of cytotoxic T cells.

PROCESS Figure

PROCESS Figure 14.16 **Proliferation of Cytotoxic T Cells**

Cytotoxic T cells increase in number in response to an abnormal MHC class I molecule.

How is the proliferation of cytotoxic T cells different from the proliferation of helper T cells illustrated in figure 14.11?

1. When viruses infect cells, some viral proteins are broken down and become processed antigens that are combined with MHC class I molecules and displayed on the surface of the infected cell. Cytotoxic T cells can distinguish between virally infected cells and noninfected cells because the T-cell receptor can bind to the MHC class I/viral antigen complex, which is not present on uninfected cells.
2. The cytotoxic T cell is activated when the T-cell receptor binds with the MHC class I/antigen complex.
3. Costimulation by other surface molecules, such as CD8, also occurs.
4. Helper T cells provide costimulation as well by releasing cytokines, such as interleukin-2, which stimulate activation and cell division of cytotoxic T cells.
5. Increasing the number of "daughter" helper T cells results in greater stimulation of cytotoxic T cells. In cell-mediated responses, helper T cells are activated and stimulated to divide in the same fashion as in antibody-mediated responses (see figure 14.11).

After cytotoxic T cells are activated by an antigen on the surface of a target cell, they undergo a series of divisions to produce additional cytotoxic T cells and memory T cells (figure 14.17). The cytotoxic T cells are responsible for the immediate cell-mediated immune response, and the **memory T cells** provide a secondary response and long-lasting immunity in the same fashion as memory B cells.

Figure 14.17 APR **Stimulation and Effects of T Cells**

When activated, cytotoxic T cells form many additional cytotoxic T cells, as well as memory T cells. The cytotoxic T cells release cytokines that promote the destruction of the antigen or cause the lysis of target cells, such as virally infected cells, tumor cells, or transplanted cells. The memory T cells are responsible for the secondary response.

CLINICAL IMPACT

Use of Monoclonal Antibodies

A **monoclonal antibody** is a pure antibody preparation that is specific for only one antigen. Monoclonal antibodies are grown in laboratories and have many clinical uses. Monoclonal antibodies are produced by injecting an antigen into a laboratory animal to activate a B-cell clone against the antigen. These B cells are removed from the animal and fused with tumor cells. The resulting cells have two ideal characteristics: (1) They produce only one (mono) specific antibody because they are derived from one B-cell clone, and (2) they divide rapidly because they are derived from tumor cells. The result is many cells producing a specific antibody.

Monoclonal antibodies are used for determining pregnancy and for diagnosing diseases such as gonorrhea, syphilis, hepatitis, rabies, and cancer. These tests are specific and rapid because the monoclonal antibodies bind only to the antigen being tested. Monoclonal antibodies were initially hailed as "magic bullets" because of their potential for delivering drugs to cancer cells (see section 14.8, "Immunotherapy"). This potential is now being realized, as over 20 monoclonal antibodies are being used to treat diseases, including some types of cancer, and hundreds more monoclonal antibodies are in clinical trials.

Cytotoxic T cells have two main effects:

1. They release cytokines that activate additional components of the immune system. For example, some cytokines attract innate immune cells, especially macrophages. These cells are then responsible for phagocytosis of the antigen and the production of an inflammatory response. Cytokines also activate additional cytotoxic T cells, which increases the effectiveness of the cell-mediated response.
2. Cytotoxic T cells can come in contact with other cells and kill them. Virally infected cells have viral antigens, tumor cells have tumor antigens, and tissue transplants have foreign antigens that can stimulate cytotoxic T-cell activity. The cytotoxic T cells bind to the antigens on the surfaces of these cells and cause the cells to lyse.

14.6 ACQUIRED IMMUNITY

Learning Outcome *After reading this section, you should be able to*

A. Explain the four ways that adaptive immunity can be acquired.

There are four ways to acquire adaptive immunity: (1) active natural, (2) active artificial, (3) passive natural, and (4) passive artificial (figure 14.18). **Active immunity** results when an individual is exposed to an antigen (either naturally or artificially) and the response of the individual's own immune system is the cause of the immunity. **Passive immunity** occurs when another person or an animal develops immunity and the immunity is transferred to a nonimmune individual. *Natural* and *artificial* refer to the method of exposure or antibody transfer. *Natural* implies that contact with the antigen or transfer of antibodies occurs as part of everyday living and is not deliberate. *Artificial* implies that deliberate introduction of an antigen or antibody into the body has occurred.

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Figure 14.18 **Ways to Acquire Adaptive Immunity**
Adaptive immunity can be acquired actively or passively. Each of these pathways also involves natural and artificial means of acquiring adaptive immunity.

Active Natural Immunity

Active natural immunity results from natural exposure to an antigen, such as a disease-causing microorganism, that stimulates the immune system to respond against the antigen. Because the individual is not immune during the first exposure, he or she usually develops the symptoms of the disease.

Active Artificial Immunity

In **active artificial immunity,** an antigen is deliberately introduced into an individual to stimulate the immune system. This process is called **vaccination** (vak-sih-NAY-shun), and the introduced antigen is a **vaccine** (vak-SEEN). A vaccine is usually administered by injection. Examples of vaccinations are the DTP injection against diphtheria, tetanus, and pertussis (whooping cough) and the MMR injection against mumps, measles, and rubella (German measles).

The vaccine usually consists of part of a pathogen, either a dead microorganism or a live, altered one. The antigen has been changed so that it will stimulate an immune response but will not cause the disease symptoms. Because active artificial immunity produces long-lasting immunity without disease symptoms, it is the preferred method of acquiring adaptive immunity.

Passive Natural Immunity

Passive natural immunity results when antibodies are transferred from a mother to her child across the placenta before birth. During her life, the mother has been exposed to many antigens, either naturally or artificially, and she has antibodies against many of these antigens, which protect her and the developing fetus against disease. Some of the antibodies (IgG) can cross the placenta and enter the fetal blood. Following birth, the antibodies protect the baby for the first few months. Eventually, the antibodies break down, and the baby must rely on its own immune system. If the mother breastfeeds her baby, antibodies (IgA) in the mother's milk also provide protection for the baby.

Passive Artificial Immunity

Passive artificial immunity involves the collecting of antibodies from one source and introducing them to an infected individual, usually through injection. Achieving passive artificial immunity begins with vaccinating an animal, such as a horse. After the animal's immune system responds to the antigen, antibodies are removed from the animal and injected into the human requiring immunity. Alternatively, a human who has developed immunity through natural exposure or vaccination can serve as a source of antibodies. Passive artificial immunity provides immediate protection because the antibodies either directly or indirectly destroy the antigen. Passive artificial immunity is therefore the preferred treatment when not enough time is available for the individual to develop his or her own active immunity. However, the technique provides only temporary immunity because the antibodies are used or eliminated by the recipient.

Antibodies that provide passive artificial immunity are referred to by the general term **antiserum** because the antibodies are found in serum, which is plasma minus the clotting factors. Antisera are available against microorganisms that cause disease, such as rabies, hepatitis, and measles; bacterial toxins, such as those that cause tetanus, diphtheria, and botulism; and venoms from certain snakes and spiders.

14.7 IMMUNOTHERAPY

Learning Outcome *After reading this section, you should be able to*

A. Define and give examples of immunotherapy.

Knowledge of how the immune system operates has produced two fundamental benefits: (1) an understanding of the cause and progression of many diseases and (2) the development or proposed development of methods to prevent, stop, or even reverse diseases.

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SYSTEMS PATHOLOGY

Systemic Lupus Erythematosus

Background Information

Lucy was diagnosed with lupus when she was 25. **Systemic lupus erythematosus (SLE)** (LOO-pus er-i-thee-mah-TOH-sus) is a disease in which tissues and cells are damaged by the immune system (figure 14.19). The name describes the skin rash that is characteristic of the disease (figure 14.20). The term *lupus* literally means "wolf" and originally referred to eroded (as if gnawed by a wolf) lesions of the skin. *Erythematosus* refers to redness of the skin resulting from inflammation. Unfortunately, as the term *systemic* implies, the disorder is not confined to the skin but can affect tissues and cells throughout the body. Another systemic effect is the presence of low-grade fever in most cases of active SLE.

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Figure 14.19 Systems Interactions: Systemic Lupus Erythematosus (SLE)

SLE is an autoimmune disease that is not isolated to one system. The diagram illustrates how the systems of the body are affected by SLE.

Figure 14.20 Skin Lesions Are Common in Individuals with SLE

Inflammation in the skin caused by systemic lupus erythematosus results in the characteristic "butterfly rash" on the face.

BSIP/Science Source

SLE is an autoimmune disorder in which a large variety of antibodies are produced that recognize self-antigens. The combination of the antibodies with self-antigens forms immune complexes that circulate throughout the body and are deposited in various tissues, where they stimulate inflammation and tissue destruction. Thus, SLE can affect many body systems.

The cause of SLE is unknown. The most popular hypothesis suggests that a viral infection disrupts the function of the T cells that normally prevent an immune response to self-antigens. Genetic factors probably contribute to the development of the disease. The likelihood of developing SLE is much higher if a family member also has it.

Approximately 1 out of 2000 individuals in the United States has SLE. The first symptoms usually appear between 15 and 25 years of age, affecting women approximately nine times as often as men. The progress of the disease is unpredictable, with flare-ups followed by periods of remission. The survival after diagnosis is greater than 90% after 10 years. The most frequent causes of death are kidney failure, CNS dysfunction, infections, and cardiovascular disease.

There is no cure for SLE, nor is there one standard of treatment because the course of the disease is highly variable, and patient histories differ widely. Treatment usually begins with mild medications and proceeds to increasingly potent therapies as conditions warrant.

Table 14.3 REPRESENTATIVE DISEASES AND DISORDERS: Lymphatic System

Condition	Description
LYMPHATIC SYSTEM	
Lymphedema (LIMF-e-DEE-mah)	Abnormal accumulation of lymph in tissues, often the limbs; 70%–90% cases in women; can be caused by developmental defects, disease, or damage to the lymphatic system
Lymphoma (lim-FOH-mah)	Cancer of lymphocytes that often begins in lymph nodes; immune system becomes depressed, with increased susceptibility to infections
IMMUNE SYSTEM	
Immediate Allergic Reactions	Symptoms occur within a few minutes of exposure to an antigen because antibodies are already present from prior exposure
Asthma (AZ-mah)	Antigen combines with antibodies on mast cells or basophils in the lungs, which then release inflammatory chemicals that cause constriction of the air tubes, so that the patient has trouble breathing
Anaphylaxis (AN-ah-fi-LAK-sis, AN-ah-fih-LAK-sis)	Systemic allergic reaction, often resulting from insect stings or drugs such as penicillin; chemicals released from mast cells and basophils cause systemic vasodilation, increased vascular permeability, drop in blood pressure, and possibly death
Delayed Allergic Reactions	Symptoms occur in hours to days following exposure to the antigen because these types of reactions involve migration of T cells to the antigen, followed by release of cytokines
Immunodeficiencies	
Severe combined immunodeficiency (SCID)	Congenital; both B cells and T cells fail to form; unless patient kept in a sterile environment or provided with a compatible bone marrow transplant, death from infection results
Acquired immunodeficiency syndrome (AIDS)	Life-threatening disease caused by the human immunodeficiency virus (HIV)

Apply It 4

The red lesion Lucy developed on her arm is called purpura (PUR-pyoo-ra), and it is caused by bleeding into the skin. The lesions

gradually change color and disappear in 2 or 3 weeks. Explain how SLE produces purpura.

Immunotherapy treats disease by altering immune system function or by directly attacking harmful cells. Some approaches attempt to boost immune system function in general. For example, administering cytokines or other agents can promote inflammation and activate immune cells, which can help destroy tumor cells. On the other hand, sometimes inhibiting the immune system is helpful. For example, multiple sclerosis is an autoimmune disease in which the immune system treats self-antigens as foreign antigens, destroying the myelin that covers axons. A type of cytokine called interferon beta blocks the expression of MHC molecules that display self-antigens and is used to treat multiple sclerosis.

Some immunotherapy takes a more specific approach. For example, vaccination can prevent many diseases (see section 14.6, "Acquired Immunity"). The ability to produce monoclonal antibodies can result in effective therapies for treating tumors. If an antigen unique to tumor cells can be found, then monoclonal antibodies can be used to deliver radioactive isotopes, drugs, toxins, enzymes, or cytokines that kill the tumor cell directly or activate the immune system to kill the cell. Unfortunately, so far researchers have found no antigen on tumor cells that is not also present on normal cells. Nonetheless, this approach can be useful if damage to normal cells is minimal.

Some uses of monoclonal antibodies to treat tumors are yielding promising results. For example, monoclonal antibodies with radioactive iodine (^{131}I) have been found to cause the regression of B-cell lymphomas while producing few side effects. Herceptin, a monoclonal antibody, binds to a growth factor receptor that is overexpressed in 25–30% of primary breast cancers. The antibody "tags" cancer cells, which are then lysed by natural killer cells. Herceptin slows disease progression and increases survival time, but it is not a cure for breast cancer.

Many other immunotherapy approaches are being studied, and more treatments that use the immune system are sure to develop in the future.

EFFECTS OF AG

Aging appears to have little effect on the lymphatic system's ability to remove fluid from tissues, absorb lipids from the digestive tract, or remove defective red blood cells from the blood. However, aging has a severe impact on the immune system.

With age, people eventually lose the ability to produce new, mature T cells in the thymus. By age 40, much of the thymus has been replaced

with adipose tissue, and after age 60, the thymus decreases in size to the point that it can be difficult to detect. While the number of T cells remains stable in most individuals due to the replication (not maturation) of T cells in lymphatic tissues, the T cells are less functional. In many individuals, the ability of helper T cells to proliferate in response to antigens decreases. Thus, antigen exposure produces fewer helper T cells, which results in less stimulation of B cells and cytotoxic T cells. Consequently, both antibody-mediated immunity and cell-mediated immunity responses to antigens decrease with age.

Both primary and secondary antibody responses decrease with age. More antigen is required to produce a response, the response is slower, less antibody is produced, and fewer memory cells result. Thus, a person's ability to resist infections and develop immunity decreases.

The ability of cell-mediated immunity to resist intracellular pathogens also decreases with age. For example, the elderly are more susceptible to influenza (flu) and should be vaccinated every year. Some pathogens cause disease but are not eliminated from the body; with age, decreased immunity can lead to reactivation of the pathogen. An example is the virus that causes chickenpox in children, which can remain latent within nerve cells, even though the disease seems to have disappeared. Later in life, the virus can leave the nerve cells and infect skin cells, causing painful lesions known as herpes zoster, or shingles.

Autoimmune disease occurs when immune responses destroy otherwise healthy tissue. There is very little increase in the number of new-onset autoimmune diseases in the elderly. However, the chronic inflammation and immune responses that began earlier in life have a cumulative, damaging effect. Likewise, the increased incidence of cancer in the elderly is likely to be caused by a combination of repeated exposure to and damage from cancer-causing agents and decreased immunity.

SUMMARY

14.1 Functions of the Lymphatic System

The lymphatic system maintains fluid balance in tissues, absorbs lipids from the small intestine, and defends against pathogens.

14.2 Anatomy of the Lymphatic System

The lymphatic system consists of lymph, lymphocytes, lymphatic vessels, lymph nodes, tonsils, the spleen, and the thymus.

Lymphatic Capillaries and Vessels

1. Lymphatic vessels carry lymph away from tissues. Valves in the vessels ensure the one-way flow of lymph.
2. Skeletal muscle contraction, contraction of lymphatic vessel smooth muscle, and thoracic pressure changes move the lymph through the vessels.
3. The thoracic duct and right lymphatic duct empty lymph into the blood.

Lymphatic Organs

1. Lymphatic tissue produces lymphocytes when exposed to foreign substances, and it filters lymph and blood.
2. The tonsils protect the openings between the nasal and oral cavities and the pharynx.
3. Lymph nodes, located along lymphatic vessels, filter lymph.
4. The white pulp of the spleen responds to foreign substances in the blood, whereas the red pulp phagocytizes foreign substances and worn-out red blood cells. The spleen also functions as a reservoir for blood.
5. The thymus processes lymphocytes that move to other lymphatic tissue to respond to foreign substances.

Overview of the Lymphatic System

The lymphatic system removes fluid from tissues, absorbs lipids from the small intestine, and produces B cells and T cells, which are responsible for much of immunity.

14.3 Immunity

1. Immunity is the ability to resist the harmful effects of pathogens.
2. Immunity is classified as innate or adaptive.

14.4 Innate Immunity

Physical Barriers

1. The skin and mucous membranes are barriers that prevent microorganisms from entering the body.
2. Tears, saliva, and urine wash away microorganisms.

Chemical Mediators

1. Chemical mediators kill pathogens, promote phagocytosis, and increase inflammation.

2. Lysozyme in tears and complement in plasma are examples of chemicals involved in innate immunity.
3. Interferons prevent the replication of viruses.

White Blood Cells

1. Chemotaxis is the ability of cells to move toward pathogens or sites of tissue damage.
2. Neutrophils are the first phagocytic cells to respond to pathogens.
3. Macrophages are large phagocytic cells that are active in the latter part of an infection. Macrophages are positioned at sites where pathogens may enter tissues.
4. Basophils and mast cells promote inflammation. Eosinophils also play a role in inflammation associated with allergic reactions.
5. Natural killer cells lyse tumor cells and virus-infected cells.

Inflammatory Response

1. Chemical mediators cause vasodilation and increase vascular permeability, allowing chemicals to enter damaged tissues. Chemicals also attract phagocytes.
2. The amount of chemical mediators and phagocytes increases until the cause of the inflammation is destroyed. Then the tissues undergo repair.
3. Local inflammation produces redness, heat, swelling, pain, and loss of function. Symptoms of systemic inflammation include an increase in neutrophil numbers, fever, and shock.

14.5 Adaptive Immunity

1. Antigens are molecules that stimulate adaptive immunity.
2. B cells are responsible for antibody-mediated immunity; T cells are involved with cell-mediated immunity.

Origin and Development of Lymphocytes

1. B cells and T cells originate in red bone marrow. T cells are processed in the thymus, and B cells are processed in red bone marrow.
2. B cells and T cells move to lymphatic tissue from their processing sites. They continually circulate from one lymphatic tissue to another.

Activation and Multiplication of Lymphocytes

1. B cells and T cells have antigen receptors on their surfaces. Clones are lymphocytes with the same antigen receptor.
2. Major histocompatibility complex (MHC) molecules present processed antigens to B or T cells.

3. Costimulation by cytokines, such as interleukins, and surface molecules, such as CD4, are required in addition to MHC molecules.
4. Macrophages present processed antigens to helper T cells, which divide and increase in number.
5. Helper T cells stimulate B cells to divide and differentiate into plasma cells that produce antibodies.

Antibody-Mediated Immunity

1. Antibodies are proteins. The variable region combines with antigens and is responsible for antibody specificity. The constant region activates complement or attaches the antibody to cells. The five classes of antibodies are IgG, IgM, IgA, IgE, and IgD.
2. Antibodies directly inactivate antigens or cause them to clump together. Antibodies indirectly destroy antigens by promoting phagocytosis and inflammation.
3. The primary response results from the first exposure to an antigen. B cells form plasma cells, which produce antibodies, and memory B cells.
4. The secondary (memory) response results from exposure to an antigen after a primary response. Memory B cells quickly form plasma cells and new memory B cells.

Cell-Mediated Immunity

1. Exposure to an antigen activates cytotoxic T cells and produces memory T cells.
2. Cytotoxic T cells lyse virally infected cells, tumor cells, and tissue transplants. Cytotoxic T cells produce cytokines, which promote inflammation and phagocytosis.

14.6 Acquired Immunity

1. Active natural immunity results from everyday exposure to an antigen against which the person's own immune system mounts a response.
2. Active artificial immunity results from deliberate exposure to an antigen (vaccine) to which the person's own immune system responds.
3. Passive natural immunity is the transfer of antibodies from a mother to her fetus during gestation or to her baby during breastfeeding.
4. Passive artificial immunity is the transfer of antibodies from an animal or another person to a person requiring immunity.

14.7 Immunotherapy

Immunotherapy stimulates or inhibits the immune system to treat diseases.

REMEMBERING AND UNDERSTANDING

1. List the parts of the lymphatic system, and describe the three main functions of the lymphatic system.
2. What is the function of the valves in lymphatic vessels? What causes lymph to move through lymphatic vessels?
3. Which parts of the body are drained by the right lymphatic duct and which by the thoracic duct?
4. Describe the cells and fibers of lymphatic tissue, and explain the functions of lymphatic tissue.
5. Name the three groups of tonsils. What is their function?
6. Where are lymph nodes found? What is the function of the germinal centers within lymph nodes?
7. Where is the spleen located? What are the functions of white pulp and red pulp within the spleen? What other function does the spleen perform?
8. Where is the thymus located, and what function does it perform?
9. What is the difference between innate immunity and adaptive immunity?
10. How do physical barriers and chemical mediators provide protection against pathogens? Describe the effects of complement and interferons.
11. Describe the functions of the two major phagocytic cell types of the body. What is the mononuclear phagocytic system?
12. Name the cells involved in promoting inflammation.
13. What protective function do natural killer cells perform?
14. Describe the effects that take place during an inflammatory response. What are the symptoms of local and systemic inflammation?
15. Define antigen. What is the difference between a self-antigen and a foreign antigen?
16. Which cells are responsible for antibody-mediated immunity and for cell-mediated immunity?
17. Describe the origin and development of B cells and T cells.
18. What is the function of antigen receptors and major histocompatibility proteins?
19. What is costimulation? Give an example.

20. Describe the process by which an antigen can cause an increase in helper T-cell numbers.
21. Describe the process by which helper T cells can stimulate B cells to divide, differentiate, and produce antibodies.
22. What are the functions of the variable and constant regions of an antibody?
23. Describe the direct and indirect ways that antibodies destroy antigens.
24. What are the functions of plasma cells and memory B cells?
25. Define primary and secondary responses. How do they differ from each other in regard to speed of response and amount of antibody produced?
26. Explain how cytotoxic T cells are activated.
27. What are the functions of cytotoxic T cells and memory T cells?
28. Define active natural, active artificial, passive natural, and passive artificial immunity. Give an example of each.

CRITICAL THINKING

1. A patient is suffering from edema in the right lower limb. Explain why elevation and massage of the limb help remove the excess fluid.
2. If the thymus of an experimental animal is removed immediately following birth, the animal exhibits the following characteristics:
   a. increased susceptibility to infections
   b. decreased numbers of lymphocytes
   c. greatly decreased ability to reject grafts
   Explain these observations.
3. Adjuvants are substances that slow, but do not stop, the release of an antigen from an injection site into the blood. Suppose injection A of a given amount of antigen is given without an adjuvant and injection B of the same amount of antigen is given with an adjuvant that caused the release of antigen over a period of 2 to 3 weeks. Does injection A or injection B result in the greater amount of antibody production? Explain.

4. Compare how long active immunity and passive immunity last. Explain the difference between the two types of immunity. In what situations is one type preferred over the other?
5. Tetanus is caused by bacteria (*Clostridium tetani*) that enter the body through wounds in the skin. The bacteria produce a toxin that causes spastic muscle contractions. Death often results from failure of the respiratory muscles. A patient goes to the emergency room after stepping on a nail. If the patient has been vaccinated against tetanus, he is given a

tetanus booster shot, which consists of the toxin altered so that it is harmless. If the patient has never been vaccinated against tetanus, he is given an antiserum shot against tetanus. Explain the rationale for this treatment strategy. Sometimes both a booster and an antiserum shot are given, but at different locations on the body. Explain why this is done and why the shots are given in different locations.

6. A child appears healthy until approximately 9 months of age. Then the child develops severe bacterial infections, one after another. Fortunately, the infections are successfully treated with antibiotics. When infected with measles and other viral diseases, the child recovers without difficulty. Explain.
7. Samantha developed a poison ivy rash after a camping trip. Her doctor prescribed a cortisone ointment to relieve the inflammation. A few weeks later, Samantha scraped her elbow, which became inflamed. Because she had some leftover cortisone ointment, she applied it to the scrape. Was the ointment a good idea for the poison ivy? Was it an appropriate treatment for the scrape?

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

15

Respiratory System

Respiration occurs at multiple levels. We respire when our blood travels through our lungs and picks up oxygen and drops off carbon dioxide. We also respire when that oxygen gets delivered to our cells and carbon dioxide is carried away from those cells. Finally, we respire when our cells use that oxygen to make needed energy and create carbon dioxide as waste. All levels of respiration are essential for life.

LEARN TO APPLY IT

Flashing lights at 2 a.m. alerted the neighbors that something was wrong at the Theron home. Mr. Theron, who has moderate emphysema, could not stop coughing, so his wife called 911. In the emergency room, a physician listened to Mr. Theron's respiratory sounds and concluded that his left lung had collapsed.

Apply

Explain how emphysema affected Mr. Theron's breathing, what caused his lung to collapse, and how the physician was able to detect the collapsed lung. How would a ventilator help?

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

15.1 ANATOMY OF THE RESPIRATORY SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. List the structures that compose the respiratory system.
B. Describe the structural and functional anatomy of the respiratory system.

The respiratory system consists of the structures used to acquire oxygen (O_2) and remove carbon dioxide (CO_2) from the blood. Oxygen is required for the body's cells to synthesize the chemical energy molecule, ATP. Carbon dioxide is a by-product of ATP production and must be removed from the blood. Otherwise, increased levels of CO_2 will lower the pH of the blood. The blood pH must be maintained within relatively narrow limits to maintain homeostasis.

There are seven structures that make up the respiratory system (figure 15.1). They include the following:

1. *External nose.* The external nose encloses the chamber for air inspiration. Although air can be inspired through the mouth, the mouth is part of the digestive system rather than the respiratory system.
2. *Nasal cavity.* The nasal cavity is a cleaning, warming, and humidifying chamber for inspired air.
3. *Pharynx.* The pharynx is commonly called the throat. It serves as a shared passageway for food and air.
4. *Larynx.* The larynx is frequently called the voice box. Its rigid structure helps keep the airway constantly open, or patent.
5. *Trachea.* The trachea is commonly known as the windpipe. It serves as an air-cleaning tube to funnel inspired air to each lung.
6. *Bronchi.* The bronchi are tubes that direct air into the lungs.
7. *Lungs.* Each lung is a labyrinth of air tubes and a complex network of air sacs, called alveoli, and capillaries. The air sacs are separated by walls of connective tissue containing both collagenous and elastic fibers. Each air sac is the site of gas exchange between the air and the blood.

In this chapter, we will discuss the detailed anatomy of each component of the respiratory system and the mechanisms that control breathing and gas exchange.

15.2 FUNCTIONS OF THE RESPIRATORY SYSTEM

Learning Outcome *After reading this section, you should be able to*

A. Describe the functions of the respiratory system.

Respiration, or what we call breathing, is critical for homeostasis. There are two broad aspects of respiration: (1) **ventilation,** which is simply movement of air into and out of the lungs, and (2) **respiration,** which is the diffusion of gases across cell membranes. There are two major types of respiration within the body: (1) **external respiration,** which is the movement of gases between atmospheric air in the lungs and the blood, and (2) **internal respiration,** which is the movement of gases between the blood and the body's cells.

Ventilation and respiration occur in different regions of the respiratory tract. Commonly the respiratory tract is separated into two regions: (1) the **upper respiratory tract,** which includes the structures from the nose to the larynx, and (2) the **lower respiratory tract,** which includes the structures from the trachea through the alveoli in the lungs. Infections of the upper respiratory tract

are among the top five reasons patients in the United States see their doctor. The upper and lower respiratory tract can be further subdivided between structures used strictly for ventilation and structures used for respiration. The **conducting zone** encompasses the structures from the nose to the smallest air tubes within the lungs and is strictly for ventilation. The **respiratory zone** is solely within the lungs and includes some specialized small air tubes and the alveoli. Gas exchange occurs within the respiratory zone.

For the respiratory system to accomplish gas exchange between the air and the blood, there are four simultaneous processes:

1. *Ventilation.* This is what we more commonly refer to as breathing. Air moves into and out of the respiratory passages.
2. *External respiration.* At the terminal portion of the air tubes, are tiny air sacs called alveoli. Oxygen moves out of the alveolar air and into the blood. At the same time, CO_2 diffuses out of the blood and joins the air in the alveoli.
3. *Gas transport.* Carbon dioxide and O_2 travel in the blood to and from cells.
4. *Internal respiration.* Gas exchange with the tissues involves the exit of O_2 from the blood into cells, while CO_2 exits cells to enter the blood.

Sometimes, it could be confusing to hear the term *respiration* alone because it also refers to cellular metabolism, or **cellular respiration** (discussed in chapter 17); in fact, the two processes are related. Breathing provides the O_2 needed in cellular respiration to make ATP from glucose. Breathing also rids the body of potentially toxic CO_2, which is produced during cellular respiration.

In addition to respiration, the respiratory system performs the following functions:

1. *Regulation of blood pH.* The respiratory system can alter blood pH by changing blood CO_2 levels.
2. *Production of chemical mediators.* The lungs produce an enzyme called angiotensin-converting enzyme (ACE), which is an important component of blood pressure regulation (discussed in chapter 18).
3. *Voice production.* Air moving past the vocal folds makes sound and speech possible.
4. *Olfaction.* The sensation of smell occurs when airborne molecules are drawn into the nasal cavity (discussed in chapter 9).
5. *Protection.* The respiratory system provides protection against some microorganisms by preventing them from entering the body and removing them from respiratory surfaces.

Figure 15.1 APR **Respiratory System**

The upper respiratory tract consists of the external nose, nasal cavity, the pharynx (throat), and the larynx. The lower respiratory tract consists of the trachea, bronchi, and lungs.

15.3 STRUCTURES AND HISTOLOGY OF THE RESPIRATORY TRACT

Learning Outcomes *After reading this section, you should be able to*

A. Describe the anatomy of the respiratory passages, beginning at the nose and ending with the alveoli.
B. State the parts of the respiratory membrane.
C. Explain the role of the thoracic wall in respiration.
D. Describe the structure of the lungs, including the blood and lymphatic supply.
E. Explain the role of the pleura in respiration.

Structures of the upper and lower respiratory tract are well-adapted for the conduction of air through the respiratory tract. These structures move, clean, warm, and humidify the air. In the upper respiratory tract, air is moved from the external environment toward the alveoli. Once air is in the alveoli, the respiratory function of the lower respiratory tract is readily carried out due to the close contact of the alveoli with blood capillaries.

The Upper Respiratory Tract

Nose and Nasal Cavity

The **nose** consists of the external nose and the nasal cavity. The **external nose** is the visible structure that forms a prominent feature of the face. The largest part of the external nose is composed of hyaline cartilage plates. However the *bridge* of the nose, which is where eyeglasses would rest, consists of bone.

The **nasal cavity** is the open chamber inside the nose where air first enters the respiratory system. The nasal cavity begins at the anterior external openings called the **nares** (NAH-reez; sing. naris), or *nostrils*. It extends to posterior openings into the pharynx. These openings are called **choanae** (KO-a-nay; figure 15.2).

Figure 15.2 APR **Nasal Cavity and Pharynx**

(*a*) Sagittal section through the nasal cavity and pharynx. (*b*) Photograph of sagittal section of the nasal cavity.

(b) Living Art Enterprises/Science Source

The floor of the nasal cavity, which separates it from the oral cavity in the mouth, is called the **hard palate** (PAL-uht). Within the nasal cavity, the hard palate is covered by a highly vascular mucous membrane. It is this mucous membrane that helps warm and humidify inspired air. The nasal cavity is divided into right and left halves. The two halves are separated by a wall of tissue called the **nasal septum.** The anterior part of the nasal septum is composed of cartilage, while the posterior part consists of bone. A deviated nasal septum occurs when the septum bulges to one side and is a common cause of snoring (see figure 15.2).

On each side of the nasal cavity, there are three lateral bony ridges called **conchae** (KON-kee; resembling a conch shell). The conchae used to be named the turbinate bones because they act as "wind turbines," helping the air churn through the nasal cavity. In fact, people with chronic nasal congestion may have a turbinate reduction in which a surgeon performs a procedure to reduce the size of the nasal conchae. The air passes through tunnels beneath each concha. Within the superior and middle meatuses are openings from the various **paranasal sinuses** (see figure 7.11). The nasal cavity also contains the opening of a **nasolacrimal** (NAY-zoh-LAK-rim-al) **duct** for tear drainage from the surface of the eye (see chapter 9).

Sinusitis (sigh-nuh-SIGH-tis) is inflammation of the mucous membrane of a sinus, especially one or more of the paranasal sinuses. Viral infections, such as the common cold, can cause mucous

membranes to become inflamed and swollen and to produce excess mucus. As a result, the sinus opening into the nasal cavity can be partially or completely blocked. In addition, mucus accumulation within the sinus can promote the development of a bacterial infection. The combination of built-up mucus and inflamed and infected mucous membranes produces pain. Treatment of sinusitis consists of taking antibiotics to kill the bacteria, taking decongestants to promote sinus drainage, drinking fluids to maintain hydration, and inhaling steam to keep nasal passages moist.

The nasal cavity is a critical component of the respiratory system. Its primary function is as the air intake portion of the respiratory system. It is here where the majority of the warming, cleaning, and humidifying of air occurs, which is critical for effective gas exchange within the lungs. In total, the nasal cavity has five functions:

1. *Serves as a passageway for air.* The nasal cavity remains open even when the mouth is full of food.
2. *Cleans the air.* The nasal cavity is lined with hairs, which trap some of the large particles of dust in the air. The nasal septum and nasal conchae increase the surface area of the nasal cavity and make airflow within the cavity more turbulent, thereby increasing the likelihood that air will come into contact with the mucous membrane lining the nasal cavity. This mucous membrane consists of pseudostratified ciliated columnar epithelium with goblet cells. The goblet cells secrete mucus, which traps debris in the air. The cilia on the surface of the mucous membrane sweep the mucus posteriorly to the pharynx, where it is swallowed and eliminated by the acidic secretions of the stomach.
3. *Humidifies and warms the air.* Moisture is added to the air as it passes through the nasal cavity. There are two major sources for the moisture: (a) the mucous epithelium and (b) tears that drain into the nasal cavity through the nasolacrimal duct. Warm blood flowing through the mucous membrane warms the air within the nasal cavity before it passes into the pharynx, thus preventing damage to the rest of the respiratory passages due to cold air.
4. *Contains the olfactory epithelium.* The olfactory epithelium, the sensory organ for smell, is located in the most superior part of the nasal cavity (see chapter 9).
5. *Helps determine voice sound.* The nasal cavity and paranasal sinuses are resonating chambers for speech. For example, most people know immediately when you have a cold because your voice sounds different.

Pharynx

The **pharynx** (FAIR-inks), or throat, is the common opening of both the digestive and the respiratory systems. The pharynx receives air from the nasal cavity and receives air, food, and drink from the oral cavity. Inferiorly, the pharynx is connected to the respiratory system at the larynx and to the digestive system at the esophagus. There are three regions of the pharynx: (1) the nasopharynx, (2) the oropharynx, and (3) the laryngopharynx (figure 15.2*a*).

The **nasopharynx** (NAY-zoh-FAIR-inks) is the most superior portion of the pharynx. It is immediately posterior to the nasal cavity. Specifically, it is a continuation of the nasal cavity from the choanae. The nasopharynx is superior to the **soft palate.** The soft palate is an incomplete partition composed of muscle and connective tissue. It separates the nasopharynx from the middle portion of the pharynx, the oropharynx. The extension of the soft palate is called the **uvula** (YOU-vyu-lah; grape). The soft palate prevents swallowed materials from entering the nasopharynx and nasal cavity. It pushes food and other materials toward the back of the pharynx. The nasopharynx is continuous with the middle ear through the auditory tubes, openings on each side of the nasopharynx (figure 15.2*a*). Air passes through the auditory tubes to equalize air pressure between the atmosphere and the tympanic membrane. The posterior wall of the nasopharynx houses the **pharyngeal tonsil,** or *adenoids* (ADD-eh-noydz), which helps defend the body against infection (see chapter 14). An enlarged pharyngeal tonsil can interfere with normal breathing and airflow through the auditory tubes.

The **oropharynx** (OR-oh-FAIR-inks) is a continuation of the nasopharynx. The oropharynx is the middle portion of the pharynx. It is immediately posterior to the mouth and begins at the soft palate. From there, it descends to the superior portion of the larynx. Because the mouth's oral cavity and the oropharynx join, air, food, and drink all pass through the oropharynx. Moist stratified squamous epithelium lines the oropharynx and protects it against abrasion. Two groups of tonsils, called the **palatine tonsils** and the **lingual tonsil**, are located near the fauces.

The **laryngopharynx** (lah-RING-oh-FAIR-inks) is a continuation of the oropharynx. The laryngopharynx spans the posterior length of the larynx: from the most superior larynx structure, the epiglottis, to the esophagus. Food and drink pass through the laryngopharynx to the esophagus. Although most air passes from the laryngopharynx into the larynx, a small amount of air may be swallowed with food and drink. The laryngopharynx is lined with moist stratified squamous epithelium.

1. *Thyroid cartilage.* The **thyroid** (shield) **cartilage** is the largest of the cartilages. It is a single shield-shaped piece of cartilage, which is also known as the *Adam's apple.*
2. *Cricoid cartilage.* The **cricoid** (CRY-koyd; ring-shaped) **cartilage** forms the base of the larynx. It is a single piece of cartilage upon which the other cartilages rest.
3. *Epiglottis.* The **epiglottis** (ep-ih-GLOT-is; on the glottis) is a single piece of cartilage that is attached to the thyroid cartilage and projects superiorly. The epiglottis is unique among the larynx cartilages because it is a freely movable flap and is constructed of elastic cartilage rather than hyaline cartilage. It helps divert food away from the trachea opening during swallowing.
4. *Arytenoid cartilages.* The paired **arytenoid** (ar-ih-TEE-noyd; ladle-shaped) **cartilages** articulate with the superior border on the posterior of the cricoid cartilage.
5. *Corniculate cartilages.* The paired **corniculate** (kor-NIK-you-late; horn-shaped) **cartilages** are attached to the superior tips of the arytenoid cartilages.
6. *Cuneiform cartilages.* The paired **cuneiform** (KYU-nee-ih-form; wedge-shaped) **cartilages** are contained in a mucous membrane anterior to the corniculate cartilages.

Larynx

The **larynx** (LAIR-inks) is commonly known as the voice box. It is located in the anterior part of the laryngopharynx and extends from the base of the tongue to the trachea. The larynx is held in place by membranes and muscles superior to the hyoid bone (figure 15.2*a*). The rigid walls of the larynx maintain an open passageway between the pharynx and the trachea. Its rigidity is due to an outer casing of nine cartilages connected to one another by muscles and ligaments (figure 15.3). Six of the nine cartilages are paired, and three are unpaired. The following is a list of the cartilages composing the larynx:

Figure 15.3 **Anatomy of the Larynx**

The larynx is called the voice box because it houses the ligaments used for speech as well as for swallowing and other functions (figure 15.4). These ligaments include (1) the vestibular folds and (2) the vocal folds. The **vestibular folds,** or *false vocal cords,* are the superior pair of ligaments. The **vocal folds,** or *true vocal cords,* are the inferior ligaments. If the vocal folds become inflamed, **laryngitis** (lair-in-JIE-tis) occurs and the person "loses" his or her voice.

Figure 15.4 **APR Vestibular and Vocal Folds**

(*Far left*) The arrow shows the direction of viewing the vestibular and vocal folds. (*a*) The relationship of the vestibular folds to the vocal folds and the laryngeal cartilages. (*b*) Superior view of the vestibular and vocal folds as seen through a laryngoscope.

(b) CNRI/Science Source

The larynx, with its cartilages and the vestibular and vocal folds, perform four main functions:

1. Maintains an open passageway for air movements
2. Prevents swallowed materials from entering the larynx and lower respiratory tract
3. Produces sound for speech
4. Protects the lower respiratory tract from foreign materials

Functions of the Vestibular and Vocal Folds

The vocal folds are the primary source of sound production. Air moving past the vocal folds causes them to vibrate and produce sound. The force of air moving past the vocal folds determines the loudness of the sound. The frequency of vibrations determines pitch, with higher-frequency vibrations producing higher-pitched sounds and lower-frequency vibrations producing lower-pitched sounds. Skeletal muscles control the movement of the cartilages in the larynx, which changes the position and length of the vocal folds and thus the pitch of the sound. Because males usually have longer vocal folds than females, most males have lower-pitched voices. The sound produced by the vibrating vocal folds is modified by the tongue, lips, teeth, and other structures to form words.

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In addition to sound production, the vestibular and vocal folds provide the most important method for preventing swallowed materials from entering the larynx. During swallowing, food passes over the epiglottis toward the esophagus and the vestibular and vocal folds move together medially, closing the glottis. The closure of the vestibular and vocal folds can also prevent the passage of air, as when a person holds his or her breath or increases air pressure within the lungs prior to coughing or sneezing.

Understand ***Apply It 1***

Jake told his girlfriend that the roller coaster did not bother him, but during the ride he let loose with a long, high-pitched scream. Explain how the muscles that control the vocal folds and the muscles that move the epiglottis helped produce Jake's scream.

The Lower Respiratory Tract

Trachea

The **trachea** (TRAY-kee-ah) is commonly known as the windpipe. It allows air to flow into the lungs. The trachea is a membranous tube attached to the larynx and consists of dense regular connective tissue and smooth muscle (see figure 15.3). The trachea is reinforced with 15–20 C-shaped pieces of hyaline cartilage called **tracheal rings.** The tracheal rings support the trachea and prevent it from collapsing. The cartilages support the anterior and lateral sides of the trachea to protect it while maintaining an open passageway for air. The trachea has an inside diameter of 12 mm and a length of 10–12 cm, descending from the larynx to the level of the fifth thoracic vertebra (figure 15.5). The tracheal rings are incomplete circles with the thickest portion of cartilage at the anterior wall of the trachea. The posterior wall of the trachea is devoid of cartilage and contains an elastic ligamentous membrane and bundles of smooth muscle. The smooth muscle can narrow the diameter of the trachea by contracting, which aids in coughing. Narrowing the trachea's diameter causes air to move more forcefully through the trachea, helping to expel mucus and foreign objects during coughing. The esophagus lies immediately posterior to the cartilage-free posterior wall of the trachea.

Figure 15.5 APR **Anatomy of the Trachea and Lungs**

The trachea and lungs and the branching of the bronchi are shown. Each lung is surrounded by a pleural cavity, formed by the visceral and parietal pleurae.

Understand

Apply It 2

Explain what happens to the shape of the trachea when a person swallows a large mouthful of food. Why is this change of shape advantageous?

CLINICAL IMPACT

Establishing Airflow

In cases of extreme emergency, when the upper air passageway is blocked by a foreign object to the extent that the victim cannot breathe, quick action is required to save the person's life. In abdominal thrusts, also known as the **Heimlich maneuver,** the sudden application of pressure to the abdomen can force air up the trachea to dislodge the obstruction. The person who performs the maneuver stands behind the victim with his or her arms under the victim's arms and his or her hands over the victim's abdomen between the navel and the rib cage. With one hand formed into a fist, the other hand suddenly pulls the fist toward the abdomen with an accompanying upward motion. The pressure pushes up on the diaphragm and therefore increases air pressure in the lungs. If this maneuver is done properly, it causes air to flow from the lungs with sufficient force to dislodge most foreign objects.

There are other ways to establish airflow, but they should be performed only by trained medical personnel. **Intubation** is the insertion of a tube into an opening, a canal, or a hollow organ. A tube can be passed through the mouth or nose into the pharynx and then through the larynx to the trachea. Sometimes it is necessary to make an opening for the tube. The preferred point of entry in an emergency is through the membrane between

the cricoid and thyroid cartilages (see figure 15.3*a*), a procedure referred to as a **cricothyrotomy** (KRI-ko-thi-rot-o-mi). A tube is then inserted into the opening to facilitate the passage of air.

A **tracheostomy** (tray-kee-OST-oh-mee; *tracheo-* + *stoma,* mouth) is an operation to make an opening into the trachea. Usually, the opening is intended to be permanent, and a tube is inserted into the trachea to allow airflow and provide a way to remove secretions. The term **tracheotomy** (tray-kee-OT-oh-mee; *tracheo-* + *tome,* incision) refers to the actual cutting into the trachea (although sometimes the terms *tracheostomy* and *tracheotomy* are used interchangeably). It is not advisable to enter the air passageway through the trachea in emergency cases because arteries, nerves, and the thyroid gland overlie the anterior surface of the trachea.

MICROBES IN YOUR BODY

Whooping Cough

Whooping cough, or pertussis, is a serious bacterial infection of the tracheobronchial tree, caused by the bacterium *Bordetella pertussis* (*B. pertussis; -tussis,* cough). Whooping cough is highly contagious and spreads through inhalation of airborne droplets or contact with droplet-covered surfaces. It is estimated that each newly infected person will pass the disease on to over 10 other people. After the incubation phase, a severe cough develops that consists of bouts of intense coughing, which can cause vomiting, lack of sufficient gas exchange during the coughing episode, followed by a loud inspiratory high-pitched sound, or "whoop." The coughing stage can last 10 weeks or more, but full recovery does not occur for another 2–3 months. The most severely affected patients are infants under 6 months of age, 50% of whom will require hospitalization. Infants and children under 6–7 years of age are also the most likely to develop serious side effects, which include development of pneumonia, apnea (interrupted breathing), seizures, brain hemorrhage, and even death by asphyxiation (suffocation).

B. pertussis affects both the respiratory and the immune systems simultaneously in two major ways: (1) by directly attacking the ciliated epithelium in the tracheobronchial tree and (2) by avoiding the effects of complement. In chapter 14, you learned that the tracheobronchial tree contributes to innate immunity by providing both a mechanical and a chemical barrier to invading pathogens. The mechanical barrier is formed by a mucus-producing, ciliated epithelium. The cilia constantly sweep debris and bacteria-laden mucus toward the pharynx to be swallowed. The chemical barrier is provided by activation of the complement system by roaming macrophages in the mucosal lining of the tracheobronchial tree.

The most effective method to avoid whooping cough is vaccination. Prior to the 1940s and 1950s, whooping cough was a leading cause of infant death. Then in the 1940s, development of a universal vaccine caused a sharp drop in the number of U.S. whooping cough incidences and outbreaks. However, starting in the 1980s, the number of whooping cough cases began rising to levels not seen in over 60 years. Research has shown that the increase in whooping cough incidence is most likely due to several factors, all of which center around vaccination. These factors prompted the Centers for Disease Control and Prevention (CDC) to recommend a T_{dap} booster (a vaccine for tetanus, diphtheria, and acellular pertussis given to adolescents and adults) for all pregnant women past the 20th week of gestation. Both the failure to vaccinate and the decreased vaccination rate (completion of all recommended doses) of infants and children have allowed *B. pertussis* to circulate freely throughout the population. Now *B. pertussis* has genetically adapted, so that it can avoid attack by our immune system even more effectively. In other words, the relatively recent increased number of cases has led to a decreased sensitivity of *B. pertussis* to the current vaccine. Development of a new, more effective vaccine to be given to all unvaccinated people may help eradicate this horrible disease.

A mucous membrane lines the trachea. The membrane's goblet cells produce mucus, which traps inspired dust, bacteria, and other foreign matter. The ciliated epithelium then moves the mucus and foreign matter into the larynx. From the larynx the foreign matter enters the pharynx and is swallowed. Constant, long-term irritation to the trachea, as occurs in smokers, can cause the tracheal epithelium to become moist stratified squamous epithelium that lacks cilia and goblet cells. This transition prevents the normal function of the tracheal epithelium.

Bronchi

The trachea divides to form two smaller tubes called **main bronchi,** or *primary bronchi* (BRONG-kigh; sing. bronchus, BRONG-kuss; windpipe), each of which extends to a lung. At the location

where the trachea divides into the two main bronchi is a ridge of cartilage called the **carina** (ka-RYE-nah). The carina is an important landmark for reading x-rays. In addition, the mucous membrane of the carina is very sensitive to mechanical stimulation. If foreign matter is inspired to the level of the carina, it stimulates a powerful cough reflex. Materials in the air passageways beyond the carina do not usually stimulate a cough reflex.

Tracheobronchial Tree

The **tracheobronchial** (TRAY-kee-oh-BRONG-kee-al) **tree** consists of the trachea and the network of air tubes in the lungs (figure 15.5). The trachea divides to form a left and right main bronchus, each of which divides to form smaller and smaller bronchi. The smaller bronchi continue getting smaller until they terminate in microscopic tubes and sacs. The right main bronchus is larger in diameter and more directly in line with the trachea than the left main bronchus. Because the right main bronchus is more in line with the trachea, an inspired object is more likely to become lodged in it than in the left main bronchus. The main bronchi have cartilage rings like those in the trachea. Within each lung, there are four main classes of air passageways. Overall, approximately 16 levels of branching occur from the trachea to the smallest air tubes. The walls of each class of air passageway are supported by cartilage and smooth muscle, giving way to all smooth muscle in the smallest air passageways. In addition, each class of air passageway is lined with a type of ciliated epithelium, which functions as a mucus-cilia escalator, trapping debris from the air and moving it to the larynx. The four classes of air passageways, listed from largest to smallest, are the following:

1. *Lobar bronchi.* The **lobar bronchi,** or *secondary bronchi,* arise directly from the main bronchi. In the lobar bronchi, the C-shaped cartilage rings are replaced with cartilage plates. Smooth muscle forms a layer between the cartilage and mucous membrane. The lobar bronchi are lined with pseudostratified ciliated columnar epithelium, which slowly changes as the tubes get smaller and smaller. In the left lung, there are two lobar bronchi. In the right lung, there are three lobar bronchi. Each lobar bronchus supplies its own section of each lung, which are called lobes.
2. *Segmental bronchi.* The **segmental bronchi,** or *tertiary bronchi,* supply subdivisions within each lung lobe, which are called bronchopulmonary segments. As the bronchi become smaller, the cartilage becomes sparse, and smooth muscle becomes more abundant.
3. *Bronchioles.* The **bronchioles** result from continued branching of the segmental bronchi. Bronchioles are less than 1 mm in diameter and have less cartilage and more smooth muscle. The larger bronchioles are lined with ciliated simple columnar epithelium.
4. *Terminal bronchioles.* The **terminal bronchioles** arise from several subdivisions of bronchioles. The terminal bronchioles have no cartilage in their walls, but the smooth muscle layer is prominent. The terminal bronchioles are lined with ciliated simple cuboidal epithelium.

Changes in Air Passageway Diameter

The bronchi and bronchioles are capable of changing their diameter. The smooth muscle layer in them can relax and contract. **Bronchodilation** occurs when the smooth muscle relaxes, making the bronchiole diameter larger. **Bronchoconstriction** occurs when the smooth muscle contracts, making the bronchiole diameter smaller. This works in the same way as vasoconstriction and vasodilation. The flow of air decreases when the resistance to airflow is increased by conditions that reduce the diameter of the respiratory passageways. The resistance to airflow is proportional to the diameter of a tube. Thus, a small change in diameter results in a large change in resistance, which greatly decreases airflow. For example, during exercise bronchodilation occurs, reducing the resistance to airflow, which increases air movement. However, during an **asthma attack,** there is severe bronchoconstriction. The bronchoconstriction decreases the diameter of the airways, which increases resistance to airflow and greatly reduces air movement. In severe cases, air movement can be so restricted that the patient dies. Fortunately, medications, such as **albuterol** (al-BYU-ter-ol),

help counteract the effects of an asthma attack by promoting smooth muscle relaxation in the walls of terminal bronchioles, so that air can flow more freely.

Alveoli

Thus far, all of the lower respiratory tract structures we've discussed have functioned only for ventilation, or within the conducting zone. Respiration can occur only where gas exchange between inspired air and the blood is possible. The sites of external respiration are the alveoli. **Alveoli** (al-VEE-oh-lie; hollow cavities) are small, air-filled chambers where the air and the blood come into close contact with each other (figure 15.6). From the terminal bronchioles to the alveoli, there are multiple levels of branching. In order from largest to smallest these branches are:

1. *Respiratory bronchioles.* The **respiratory bronchioles** have a few attached alveoli. As the respiratory bronchioles divide to form smaller respiratory bronchioles, the number of attached alveoli increases.
2. *Alveolar ducts.* The **alveolar** (al-VEE-oh-lar) **ducts** arise from the respiratory bronchioles. The alveolar ducts are like long, branching hallways with many open doorways. The "doorways" open into alveoli. Eventually, the number of alveoli becomes so large that the wall of the alveolar duct becomes just a series of alveoli.
3. *Alveolar sacs.* **Alveolar sacs** are chambers connected to two or more alveoli at the end of an alveolar duct.

Figure 15.6 APR **Bronchioles and Alveoli**

A terminal bronchiole branches to form respiratory bronchioles, which give rise to alveolar ducts. Alveoli connect to the alveolar ducts and respiratory bronchioles. The alveolar ducts end as two or three alveolar sacs.

The tissue surrounding the alveoli contains elastic fibers, which allow the alveoli to expand during inspiration and recoil during expiration. The alveolar ducts and alveoli consist of simple squamous epithelium. Although the epithelium of the alveoli and respiratory bronchioles is not ciliated, debris from the air can be removed by macrophages that move over the surfaces of the cells.

Alveolar Structure

Approximately 300 million alveoli are in the two lungs. The average diameter of an alveolus is approximately 250 μm, and its wall is extremely thin. Two types of cells form the alveolar wall (figure 15.7*a*): (1) squamous epithelial cells and (2) surfactant-secreting cells. The thin squamous epithelial cells form 90% of the alveolar surface. Most of the gas exchange between alveolar air and the blood takes place through these cells. Surfactant-secreting cells are round or cube-shaped secretory cells that produce surfactant, which makes it easier for the alveoli to expand during inspiration (see section 15.3).

Figure 15.7 APR **Alveolus and the Respiratory Membrane**

(*a*) Section of an alveolus, showing the air-filled interior and thin walls composed of simple squamous epithelium. The alveolus is surrounded by elastic connective tissue and blood capillaries. (*b*) O_2 and CO_2 diffuse across the six thin layers of the respiratory membrane.

(a) Living Art Enterprises/Science Source

The Respiratory Membrane

The alveolar walls and surrounding pulmonary capillaries form the **respiratory membrane** in the lungs (figure 15.7*b*). The respiratory membrane is the location of external respiration. In other words, it is where O_2 enters the blood and CO_2 exits the blood. To facilitate diffusion of gases, the respiratory membrane is extremely thin; it is thinner than a sheet of tissue paper. The general respiratory membrane components are the following:

1. The alveolar cell layer
2. An interstitial space between the alveolar layer and the capillary layer
3. The capillary endothelial layer

Associated with each of the three components are secreted fluids and basement membranes. If any of these components were to increase in thickness, the rate of gas diffusion could be appreciably

changed. Thus, understanding the identity of all of the individual layers is helpful to understand respiration. The individual layers are:

1. A thin layer of alveolar fluid
2. The alveolar epithelium, which is a single layer of simple squamous epithelium
3. The basement membrane of the alveolar epithelium
4. A thin interstitial space
5. The basement membrane of the capillary endothelium
6. The capillary endothelium, which is a single layer of simple squamous cells

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Thoracic Wall and Muscles of Respiration

The thoracic wall consists of the (1) thoracic vertebrae, (2) ribs, (3) costal cartilages, (4) sternum, and (5) associated muscles (see chapters 6 and 7). The **thoracic cavity** is the space enclosed by the thoracic wall and the **diaphragm** (DIE-ah-fram; partition). Recall from chapter 7 that the diaphragm is a sheet of skeletal muscle separating the thoracic cavity from the abdominal cavity. The diaphragm and other skeletal muscles associated with the thoracic wall change thoracic volume during ventilation (figure 15.8). We will discuss the specific roles of the muscles of respiration during ventilation in section 15.4.

Figure 15.8 APR **Effect of the Muscles of Respiration on Thoracic Volume**
(*a*) Muscles of respiration at the end of expiration. (*b*) Muscles of respiration at the end of inspiration.

Lungs

The **lungs** are the primary organs of respiration. Based on their volume, they are among the largest organs of the body. Each lung is conical in shape, and extends from the diaphragm to a point approximately 2.5 cm superior to the clavicle. The portion of the lungs in contact with the diaphragm is the **base.** The portion of the lungs that extends above the clavicle is called the **apex.** The right lung is larger than the left and weighs an average of 620 g, whereas the left lung weighs an average of 560 g.

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The **hilum** (HIGH-lum) is an indentation on the medial surface of the lung. The hilum is where structures, such as the main bronchus, blood vessels, nerves, and lymphatic vessels, enter or exit the lung. All the structures passing through the hilum are referred to as the **root of the lung.**

The right lung has three large sections called **lobes,** while the left lung has two lobes. The lung lobes are separated by deep, prominent **fissures** on the surface of the lung. Each lung lobe is supplied by a lobar bronchus. The left lung also has a medial indentation called the **cardiac notch** (figure 15.9). This structural arrangement provides room for the heart to lie between the lungs. The lung lobes are further subdivided into **bronchopulmonary segments.** Each bronchopulmonary segment is supplied by the segmental bronchi. There are 9 bronchopulmonary segments in the left lung and 10 in the right lung. The bronchopulmonary segments are separated from each other by connective tissue partitions, which are not visible as surface fissures. Individual diseased bronchopulmonary segments can be surgically removed because major blood vessels and bronchi do not cross the connective tissue partitions. This leaves the rest of the lung relatively intact. The bronchopulmonary segments are even further subdivided into **lobules** by partial walls of connective tissue. Bronchioles supply each lobule.

Figure 15.9 **Lungs, Lung Lobes, and Bronchi**
The right lung is divided into three lobes by the horizontal and oblique fissures. The left lung is divided into two lobes by the oblique fissure. A main bronchus supplies each lung, a lobar bronchus supplies each lung lobe, and segmental bronchi supply the bronchopulmonary segments (not visible).

Blood Supply to the Lungs

Blood that has passed through the lungs and picked up O_2 is called **oxygenated blood,** and blood that has passed through the tissues and released some of its O_2 is called **deoxygenated blood.** There are two blood flow routes to the lungs: (1) blood flow to the alveoli and (2) blood flow to the tissues of the bronchial tree. The major route takes deoxygenated blood to the alveoli in the lungs, where it is oxygenated (see chapter 13). To get to the alveoli, the deoxygenated blood flows through pulmonary arteries to pulmonary capillaries. In the capillaries, the blood becomes oxygenated and returns to the heart through pulmonary veins. The second route takes oxygenated blood to the tissues of the bronchi down to the respiratory bronchioles.

Lymphatic Supply to the Lungs

The lungs have two lymphatic supplies: (1) the superficial lymphatic vessels and (2) the deep lymphatic vessels. The **superficial lymphatic vessels** are deep to the connective tissue that surrounds each lung, called the **visceral pleura.** These vessels drain lymph from the superficial lung tissue and the visceral pleura. The **deep lymphatic vessels** follow the bronchi. These vessels drain lymph from the bronchi and associated connective tissues. There are no lymphatic vessels located in the walls of the alveoli. Both the superficial and deep lymphatic vessels exit the lung at the hilum.

Phagocytic cells within the lungs phagocytize debris and other foreign materials from inspired air and move them to the lymphatic vessels. In an older person, especially one who smokes or has lived

most of his or her life in a city with air pollution, these particles accumulate and cause the surface of the lungs to become gray or black. Though the lymphatic vessels primarily serve as a way to remove harmful substances from the lung tissue, cancer cells from the lungs can spread to other parts of the body through the lymphatic vessels.

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Pleura

The lungs are contained within the thoracic cavity. There are two pleural cavities within the thoracic cavity. Each pleural cavity houses one lung. The **pleural** (PLUR-al; relating to the ribs) **cavities** are lined with a serous membrane (figure 15.10). The serous membrane that covers the inner thoracic wall, the superior surface of the diaphragm, and the mediastinum is called the **parietal pleura.** At the hilum, the parietal pleura is continuous with the visceral pleura, which covers the surface of the lung.

Figure 15.10 APR **Pleural Cavities and Membranes**
Transverse section of the thorax, showing the relationship of the pleural cavities to the thoracic organs. Each lung is surrounded by a pleural cavity. The parietal pleura lines the wall of each pleural cavity, and the visceral pleura covers the surface of the lungs. The space between the parietal and visceral pleurae is small and filled with pleural fluid.

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15.4 BEHAVIOR OF GASES

Learning Outcomes *After reading this section, you should be able to*

A. Explain the role of the muscles of respiration in respiration.
B. Explain partial pressure and its relationship to the concentration of gases in the body.
C. List the pulmonary volumes and capacities, and define each of them.
D. Distinguish between anatomical dead space and physiological dead space.
E. Define *alveolar ventilation.*

As we've stated, the process of breathing is twofold: ventilation and respiration. To understand each of these mechanisms, we must examine the relationships governing the movement of gases.

Behavior of Gases and Ventilation

Ventilation, as we described earlier, is simply the movement of air into and out of the lungs. There are two primary aspects to ventilation: (1) actions of the muscles of respiration and (2) air pressure gradients.

Muscles of Respiration

The function of the muscles of respiration is to change the volume of the thoracic cavity, which allows for air to flow into and out of the lungs. There are several **muscles of inspiration** that act to increase the volume of the thoracic cavity. They include the (1) diaphragm, (2) external intercostals, (3) pectoralis minor, and (4) scalene muscles. The **muscles of expiration** are the muscles that decrease thoracic volume by depressing the ribs and sternum. These are the (1) internal intercostals and (2) transverse thoracis, with assistance from the abdominal muscles. Although the internal intercostals and the transverse thoracis are most active during expiration, and the external intercostals are most active during inspiration, the primary function of these muscles is to stiffen the thoracic wall by contracting at the same time. In this way, they prevent the thoracic cage from collapsing inward during inspiration.

Muscles of Inspiration

During inspiration, the thoracic cavity volume increases. Downward movement of the diaphragm upon contraction is responsible for approximately two-thirds of the thoracic volume increase. The diaphragm is dome-shaped, and the base of the dome attaches to the inner circumference of the inferior thoracic cage (see figure 15.8*a*). The top of the dome is a flat sheet of connective tissue called the **central tendon.** In normal, quiet inspiration, contraction of the diaphragm causes the central tendon to move downward. There is very little change in the overall shape of the diaphragm. This downward movement is facilitated by relaxation of the abdominal muscles, which moves the abdominal organs out of the way. This is noticeable when your hands rest on your stomach. However, as the depth of inspiration increases, the abdominal organs prevent the central tendon from moving downward. Continued contraction of the diaphragm causes it to flatten as the lower ribs are elevated.

The remaining muscles of inspiration, such as the external intercostals, increase thoracic volume by elevating the ribs. As the ribs are elevated, the costal cartilages allow lateral rib movement and lateral expansion of the thoracic cavity. The ribs slope downward from the vertebrae to the sternum, and elevation of the ribs also increases the front-to-back dimension of the thoracic cavity.

Muscles of Expiration

During expiration, the thoracic cavity volume decreases. During quiet breathing, expiration is a passive process due to significant amounts of elastic tissue in the thorax wall and the lungs. When tension is removed, the thorax wall and the lungs spring back into a smaller, relaxed state. In addition, the diaphragm relaxes, which causes it to move upward. Also, the external intercostals relax and the ribs move downward. Contractions of abdominal muscles also cause the thoracic cavity volume to decrease and push the abdominal organs upward into the diaphragm, which moves it superiorly.

Muscles of Respiration in Quiet Breathing Compared with Labored Breathing

Several differences can be recognized between normal, quiet breathing and labored breathing. During labored inspiration, more air moves into the lungs because all of the inspiratory muscles are active. They contract more forcefully than during quiet breathing, which causes a greater increase in thoracic volume (see figure 15.8*b*). During labored expiration, more air moves out of the lungs due

to the forceful contraction of the internal intercostals and the abdominal muscles. This produces a more rapid and greater decrease in thoracic volume than would be produced by the passive recoil of the thorax and lungs. To demonstrate this, place your hand on your stomach and pretend to blow out the candles on a birthday cake.

The Relationship Between Pressure Gradients and Ventilation

In order to fully understand why increasing thoracic cavity volume allows inspiration to occur, it is necessary to recognize the relationship between pressure and volume.

Pressure and Volume

The relationship between pressure and volume is an inverse one. That is to say that as the volume of a container increases, the pressure in that container decreases.

Thus, upon inspiration, the air pressure within the thoracic cavity decreases. Conversely, upon expiration, the air pressure within the thoracic cavity increases because the volume of the thoracic cavity decreases.

Pressure Gradients and Airflow

During inspiration, air flows into the lungs down its pressure gradient. During expiration, air flows out of the lungs down its pressure gradient. This pressure gradient is provided, in part, by atmospheric pressure—the combined force of all the gases that make up the air we breathe.

Air moves through tubes because of a pressure difference: Air moves from areas of higher pressure to areas of lower pressure. For example, during inspiration, air pressure outside the body is greater than air pressure in the alveoli, and air flows into the body through the trachea and bronchi to the alveoli.

In addition, as we will discuss, the greater the pressure difference, the faster the flow rate. If the pressure difference decreases, the flow rate also decreases. For example, at higher altitudes, atmospheric pressure is lower than at sea level, making the pressure difference less. The decrease in the pressure gradient between the atmospheric air and our alveoli is why it seems harder to breathe at high altitudes.

Measurement of Lung Function

Sometimes, a person's lungs do not move sufficient amounts of air to support normal activities. In that case, several types of medical tests can be performed to determine what might be causing the lung malfunction. The patient's measurements are then used to diagnose specific diseases and to track recovery.

Pulmonary Volumes and Capacities

Spirometry (spy-ROM-eh-tree) is the process of measuring volumes of air that move into and out of the respiratory system, and a **spirometer** (spy-ROM-eh-ter) is the device used to measure these pulmonary volumes. There are four different pulmonary volumes measured in spirometry (figure 15.11). The average values of the pulmonary volumes for a young adult male are:

1. *Tidal volume.* The **tidal volume** is the normal volume of air inspired and expired with each breath. At rest, quiet breathing results in a tidal volume of approximately 500 mL.
2. *Expiratory reserve volume.* The **expiratory reserve volume** is the amount of air that can be forcefully expired after a normal expiration (approximately 1100 mL at rest).
3. *Residual volume.* The **residual volume** is the volume of air still remaining in the respiratory passages and lungs after the most forceful expiration (approximately 1200 mL).

4. *Inspiratory reserve volume.* The **inspiratory reserve volume** is the amount of air that can be inspired forcefully after a normal inspiration (approximately 3000 mL at rest).

Figure 15.11 **Respiratory Volumes and Respiratory Capacities**
The tidal volume shown here is during resting conditions. Respiratory volumes are measurements of the volume of air moved into and out of the lungs during breathing. Respiratory capacities are the sum of two or more respiratory volumes.

The tidal volume increases when a person is more active. Because the maximum volume of the respiratory system does not change from moment to moment, an increase in tidal volume causes a decrease in the inspiratory and expiratory reserve volumes.

Pulmonary capacities are the sum of two or more pulmonary volumes (figure 15.11). Examples of pulmonary capacities are the following:

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1. **Inspiratory capacity** is the tidal volume plus the inspiratory reserve volume. It is the amount of air a person can inspire maximally after a normal expiration (approximately 3500 mL at rest).
2. **Vital capacity** is the sum of the inspiratory reserve volume, the tidal volume, and the expiratory reserve volume. It is the maximum volume of air a person can expel from the respiratory tract after a maximum inspiration (approximately 4600 mL).
3. **Functional residual capacity** is the expiratory reserve volume plus the residual volume. It is the amount of air remaining in the lungs at the end of a normal expiration (approximately 2300 mL at rest).
4. **Total lung capacity** is the sum of the inspiratory and expiratory reserve volumes plus the tidal volume and the residual volume (approximately 5800 mL).

A functional measure of lung performance is the **forced vital capacity.** This is a simple and clinically important pulmonary test. In conditions such as chronic obstructive pulmonary disease (COPD), emphysema, and chronic bronchitis, the vital capacity may not be dramatically affected, but how rapidly air is expired can be greatly decreased.

Alveolar Ventilation

Alveolar ventilation is the measure of the volume of air available for gas exchange per minute. Recall that part of the respiratory system functions solely to move air. Only a portion of each breath reaches the alveoli for gas exchange. The remaining areas where no gas exchange occurs is called the dead space. There are two types of dead space within the respiratory system: (1) anatomical dead space and (2) physiological dead space. The **anatomical dead space** areas include all the structures of the upper respiratory tract, and structures of the lower respiratory tract to the terminal bronchioles. These are all of the conducting zone areas. The volume of air in the anatomical dead space is approximately 1 mL per pound of an individual's ideal body weight. The **physiological dead space** is the combination of the anatomical dead space and the volume of any alveoli with lower than normal gas exchange.

Factors Affecting Ventilation

Gender, Age, Body Size, and Physical Fitness

Factors such as gender, age, body size, and physical conditioning cause variations in respiratory volumes and capacities from one individual to another. For example, the vital capacity of adult females is usually 20–25% less than that of adult males. The vital capacity reaches its maximum amount in young adults and gradually decreases in the elderly. Taller people usually have a greater vital capacity than people with a shorter stature, and slender people have a greater vital capacity than obese individuals. Well-trained athletes can have a vital capacity 30–40% above that of people with a sedentary lifestyle. In patients whose respiratory muscles are paralyzed by spinal cord injury or diseases such as poliomyelitis or muscular dystrophy, vital capacity can be reduced to values not consistent with survival (less than 500–1000 mL).

Disease States

In a healthy person, anatomical and physiological dead spaces are nearly the same, meaning that most alveoli are functional. However, in patients with emphysema, alveolar walls degenerate, and small alveoli combine to form larger alveoli. The result is not only fewer alveoli but also alveoli with an increased volume and decreased surface area. Although the enlarged alveoli are still ventilated, their surface area is inadequate for complete gas exchange, and the physiological dead space increases.

Behavior of Gases and Respiration

Ventilation supplies atmospheric air to the alveoli. External respiration is the next step in the process of respiration. External respiration is the diffusion of gases between the alveoli and the blood in the pulmonary capillaries. The molecules of gas move down their partial pressure gradient from the air into the blood for O_2 and from the blood into the air for CO_2.

Partial Pressure

To understand the mechanism behind the movement of O_2 into the blood and CO_2 out of the blood, we must first discuss how the amount of a gas in a mixture of gases is measured. Atmospheric pressure is due to a mixture of gases, each of which is present in a different amount. The term *pressure* is used to express the amount of each gas in a mixture. This is comparable to using the term *concentration* for solutes. The total pressure of a gas is the sum of the individual pressures of each gas. The individual pressure of each gas is called the **partial pressure.** At sea level, the pressure of all the gases in the air, or atmospheric pressure, is approximately 760 mm Hg (table 15.1).

TABLE 15.1 Partial Pressures of Gases at Sea Level

	Dry Air		Humidified Air		Alveolar Air		Expired Air	
Gases	**mm HG**	**%**	**mm HG**	**%**	**mm HG**	**%**	**mm HG**	**%**
Nitrogen	600.2	78.98	563.4	74.09	569.0	74.9	566.0	74.5
Oxygen	159.5	20.98	149.3	19.67	104.0	13.6	120.0	15.7
Carbon dioxide	0.3	0.04	0.3	0.04	40.0	5.3	27.0	3.6
Water vapor	0.0	0.0	47.0	6.20	47.0	6.2	47.0	6.2

To determine the partial pressure of each gas, its percentage is multiplied times the total pressure. The partial pressure of each gas in dry atmospheric air is as follows:

$$\begin{aligned}
&\text{Nitrogen:}\\
&(79\%)\ \mathrm{PN_2} = 0.79 \times 760 \text{ mm Hg} = 600 \text{ mm Hg}\\
&\text{Oxygen:}\\
&(21\%)\ \mathrm{Po_2} = 0.21 \times 760 \text{ mm Hg} = 160 \text{ mm Hg}\\
&\text{Carbon Dioxide:}\\
&(0.04\%)\ \mathrm{Pco_2} = 0.04 \times 760 \text{ mm Hg} = 0.3 \text{ mm Hg}\\
&\text{Water Vapor:}\\
&(0.0\%)\ \mathrm{PH_2O} = 0.0 \times 760 \text{ mm Hg} = 0.0 \text{ mm Hg}
\end{aligned}$$

Thus, atmospheric pressure of dry air at sea level is calculated using the following:

$$\text{Atmospheric air: } \mathrm{PN_2} + \mathrm{Po_2} + \mathrm{Pco_2} + \mathrm{PH_2O} = 760.3 \text{ mm Hg}$$

$$\begin{aligned}
\mathrm{PN_2} &= 600 \text{ mm Hg}\\
\mathrm{Po_2} &= 160 \text{ mm Hg}\\
\mathrm{Pco_2} &= 0.3 \text{ mm Hg}\\
\mathrm{PH_2O} &= 0.0 \text{ mm Hg}\\
&\ \ 760.3 \text{ mm Hg}
\end{aligned}$$

A common misconception is that at higher altitudes there is “less” O_2 in the air. However, this is not the case. Rather, it is total atmospheric pressure that is lower at higher altitudes than at sea level. For example, the atmospheric pressure at an elevation of 14,000 ft above sea level, the elevation of Pike’s Peak in Colorado, is about 430 mm Hg. The percentage of the air that is O_2 remains at 21%. Thus,

$$0.21 \times 430 \text{ mm Hg} = 90 \text{ mm Hg}$$

Therefore, at high altitudes your body does, in fact, react as if there were “less” O_2. However, it is the O_2 partial pressure gradient that has reduced, causing less O_2 to enter the lungs per breath. The normal initial adaptation to high altitudes is an increased breathing rate per minute, thereby allowing a sufficient amount of O_2 delivery to the lungs.

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Three factors cause differences in the composition among alveolar air, expired air, and atmospheric air: (1) Air entering the respiratory system is humidified; (2) O_2 diffuses from the

alveoli into the blood, while CO_2 diffuses from the blood into the alveoli; (3) the alveolar air is only partially replaced with atmospheric air during each inspiration.

Diffusion of Gases into and out of Liquids

Gas molecules move from the air into a liquid, or from a liquid into the air, down their partial pressure gradients. Gases move from a higher partial pressure to a lower partial pressure. When partial pressures of gases are equal between the air and a liquid, they are in equilibrium. However, to calculate the amount of a gas in a liquid, the partial pressure alone is not sufficient. The amount of the gas is also dependent on how readily a gas dissolves in the liquid. Carbon dioxide is approximately 24 times more soluble in water than O_2 is. This means that CO_2 is also more soluble than O_2 in the plasma of blood, because plasma is mostly water.

Apply It 3

As a scuba diver descends, the pressure of the water on the body prevents normal expansion of the lungs. To compensate, the diver breathes pressurized air, which has a greater pressure than air at sea level. What effect does the increased pressure have on the amount of gas dissolved in the diver's body fluids? A scuba diver who suddenly ascends to the surface from a great depth can develop decompression sickness (the bends), in which bubbles of nitrogen gas form. The expanding bubbles damage tissues or block blood flow through small blood vessels. Explain why the bubbles develop.

15.5 PHYSIOLOGY OF THE RESPIRATORY SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Describe the changes in alveolar pressure that are responsible for the movement of air into and out of the lungs.
B. Explain how surfactant and pleural pressure prevent the collapse of the lungs and how changes in pleural pressure cause changes in alveolar volume.
C. Describe the partial pressure gradients for O_2 and CO_2.
D. Explain the factors that affect gas movement through the respiratory membrane.

Now that we've established that the major driving force of ventilation is a pressure difference between atmospheric air and the thoracic cavity, let's look more closely at the step-by-step mechanisms of alveolar ventilation.

Mechanisms of Alveolar Ventilation

As we step through one respiratory cycle, or one breath, we will track the relative pressure difference between the atmosphere and the alveoli (figure 15.12). When a person inspires, the pressure in the alveoli decreases because the alveolar volume has increased. Conversely, when a person expires, the pressure in the alveoli increases because the alveolar volume has decreased. It is the pressure difference between atmospheric pressure and pressure in the alveoli that results in air movement during one respiratory cycle. The details of this process during quiet resting breathing are illustrated in figure 15.12:

1. *Alveolar pressure equals atmospheric pressure.* At the end of expiration, before the next respiratory cycle starts, atmospheric pressure and pressure in the alveoli are equal and no air moves into or out of the lungs.
2. *Alveolar pressure is less than atmospheric pressure.* As inspiration begins, contraction of inspiratory muscles increases thoracic volume, which results in expansion of the lungs and an increase in alveolar volume. The increased alveolar volume causes a decrease in intra-alveolar pressure below atmospheric pressure. Air flows into the lungs because barometric air pressure is greater than pressure in the alveoli.

❸ *Alveolar pressure again equals atmospheric pressure.* At the end of inspiration, the thorax stops expanding, the alveoli stop expanding, and pressure inside the alveoli becomes equal to barometric air pressure because of airflow into the lungs. No movement of air occurs after pressure in the alveoli becomes equal to atmospheric pressure, but the volume of the lungs is larger than it was at the end of expiration.

❹ *Alveolar pressure is greater than atmospheric pressure.* During expiration, the volume of the thorax decreases as the diaphragm relaxes, and the thorax and lungs recoil. Because thoracic volume determines alveolar volume, the smaller thoracic volume results in a corresponding decrease in alveolar volume. Thus, pressure inside the alveoli rises above atmospheric air pressure. Because pressure inside the alveoli is greater than atmospheric air pressure, air flows out of the lungs. As expiration ends, the decrease in thoracic volume stops, and the alveoli stop changing size. The process repeats, beginning at step 1.

PROCESS Figure

PROCESS Figure 15.12 APR **Alveolar Pressure Changes During Inspiration and Expiration**

The combined space of all the alveoli is represented by a large "bubble." The alveoli are actually microscopic and cannot be seen in the illustration.

Apply

How would traveling to higher altitude, where atmospheric pressure is lower, affect step 2?

Factors Affecting Alveolar Ventilation

While changes in pressure differences are the principal factors in driving alveolar ventilation, there are two other factors that influence the ability of alveoli to increase and decrease in volume. These two factors are (1) lung recoil and (2) pleural pressure.

Lung Recoil

Lung recoil is the tendency for the lungs to decrease in size after they are stretched. Imagine a stretched rubber band snapping back to its original size when released. Similarly, upon expiration, the tension on the lungs is released and they return to their original, smaller size, which compresses the alveoli. Lung recoil occurs for two reasons: (1) elastic recoil and (2) surface tension. Elastic recoil occurs because elastic fibers within the lungs and thoracic wall return to their original shape and size once the tension on them is released, just like the rubber band.

Lung recoil due to surface tension is because of hydrogen bonding within the alveoli. Alveoli are lined with an aqueous alveolar fluid, which adheres to the wall of the alveoli. However, the water molecules in the alveolar fluid are also attracted to each other toward the center of each alveolus. As hydrogen bonds form, the walls of each alveolus are pulled inward, which causes it to collapse. Collapse of the alveoli due to surface tension is prevented by the molecule **surfactant** (ser-FAK-tant; surface acting agent). Surfactant is a mixture of lipoprotein molecules produced by the surfactant-secreting cells of the alveolar epithelium. It forms a one-molecule-thick layer over the alveolar fluid, which reduces the surface tension in the alveoli. Premature infants do not produce enough surfactant. This is what is meant by the common statement that "their lungs are immature."

Too little surfactant production results in infant respiratory distress syndrome (IRDS). Surfactant is not produced in adequate quantities until about the seventh month of gestation. Thereafter, the amount produced increases as the fetus matures. Pregnant women who are likely to deliver prematurely can be given cortisol, which crosses the placenta into the fetus and stimulates surfactant synthesis.

Pleural Pressure

Pleural pressure is the pressure within the pleural cavity between the parietal pleura and the visceral pleura. Recall that the parietal and visceral pleurae are adhered to each other by pleural fluid. The pleural fluid is analogous to a thin film of water between two sheets of glass (the visceral and parietal pleurae); the glass sheets can easily slide over each other, but it is difficult to separate them. When the thoracic wall expands during inspiration, the parietal pleura exerts an outward force on the visceral pleura covering the lungs and the lungs expand. Pleural pressure pulls the lungs outward and is lower than pressure inside the alveoli. This aids in alveolar expansion.

If you have flown on a plane, or have been to the mountains, you may have experienced a situation similar to that which keeps the alveoli expanded. At higher altitudes, the atmospheric pressure is much lower than at sea level. If a bottle of liquid (such as shampoo) normally kept at sea level is rapidly taken to a high altitude, it will "explode." Because there is not as much force on the outside of the bottle at high altitude, it expands. Similarly, because the pleural pressure pulls the pleura away from the outside of the alveoli, the pressure on the alveoli is lower. The lower pressure allows the alveoli to expand. So, just as when the shampoo bottle expands when there is less pressure on the outside of it, your alveoli expand when there is less pressure on the outside of your lungs during inspiration.

If the visceral and parietal pleurae become separated, such as if the thoracic wall or lung is pierced, the lungs collapse. Because the two pleural cavities are independent, it is possible to have only one lung collapse. The separation of the visceral and parietal pleurae increases pleural pressure. This increase in pleural pressure is called a **pneumothorax** (new-moh-THOR-aks). A pneumothorax has two major possible causes: (1) penetrating trauma and (2) nonpenetrating

trauma. Types of penetrating traumas include being stabbed, getting shot by a gun, and breaking a rib. Types of nonpenetrating traumas include a blow to the chest; a medical procedure, such as insertion of a catheter to withdraw pleural fluid; disease, such as an infection or emphysema; and severe, spastic coughing. A pneumothorax may be treated by inserting a chest tube that aspirates the pleural cavity and restores a negative pressure, which can cause reexpansion of the lung. Surgery may also be necessary to close the opening into the pleural cavity. This information may help you to answer the Learn to Apply It at the beginning of this chapter.

In a **tension pneumothorax,** the pressure within the pleural cavity is always higher than barometric air pressure. Any situation where a pneumothorax occurred can lead to a tension pneumothorax. If a tear in the pleural cavity forms a tissue flap that acts as a flutter valve, it will allow air to enter the pleural cavity during inspiration but will not allow it to exit during expiration. The result is an increase in air and, as a result, pressure within the pleural cavity, which could lead to inadequate delivery of O_2 to tissues. The insertion of a large-bore needle into the pleural cavity allows air to escape and releases the pressure.

Factors Affecting Diffusion Through the Respiratory Membrane

In order for humans to utilize O_2 in the air we breathe, O_2 must be able to diffuse across the respiratory membrane into the blood. Three major factors influence the rate of gas diffusion through the respiratory membrane: (1) partial pressure gradients for O_2 and CO_2, (2) the thickness of the respiratory membrane, and (3) the surface area of the respiratory membrane.

Partial Pressure Gradients

The determining factor of gas movement direction is the partial pressure gradient for each gas. If the partial pressure gradient of a gas is higher in the alveolus, it will diffuse across the respiratory membrane into the blood. On the other hand, if the partial pressure of a gas is higher in the blood, it will diffuse across the respiratory membrane into the alveolus. When the partial pressure of a gas is greater on one side of the respiratory membrane than on the other side, net diffusion occurs from the higher to the lower partial pressure (see figure 15.7*b*). Normally, the partial pressure of oxygen (Po_2) is greater in the alveoli than in the blood of the pulmonary capillaries, and the partial pressure of carbon dioxide (Pco_2) is greater in the blood than in the alveolar air.

If faster gas exchange is needed, increasing alveolar ventilation will create a steeper partial pressure gradient for both O_2 and CO_2. The greater volume of atmospheric air exchanged with the residual volume raises alveolar Po_2 and lowers alveolar Pco_2. This promotes gas exchange. Conversely, inadequate ventilation causes a lower than normal partial pressure gradient for both O_2 and CO_2, which causes inadequate gas exchange.

Oxygen Partial Pressure Gradients

The partial pressure gradient for O_2 is into the blood from the alveoli. Once in the blood, the partial pressure gradient for O_2 is into the body's cells from the blood. Figure 15.13 illustrates the partial pressures responsible for gas exchange. The following steps describe the specific partial pressures for O_2 as it moves toward the body's cells:

❶ The Po_2 of alveolar air averages approximately 104 mm Hg. The Po_2 in the pulmonary capillaries is approximately 40 mm Hg. Thus, because the Po_2 is higher in the alveolar air, O_2 diffuses into the pulmonary capillaries, down its partial pressure gradient.

❷ Even if a person is exercising, by the time blood reaches the venous ends of the pulmonary capillaries, an equilibrium has been achieved and the Po_2 in the blood is 104 mm Hg.

❸ There is a slight decrease in the Po_2 of blood in the pulmonary veins to about 95 mm Hg. This slight decrease is due to mixing of deoxygenated blood from the bronchial veins with blood leaving the pulmonary capillaries.

4. The Po_2 of arterial blood as it arrives in the tissues is still 95 mm Hg compared to the Po_2 of the interstitial fluid, which is 40 mm Hg. The Po_2 in individual tissue cells is around 20 mm Hg. Thus, O_2 diffuses out of the capillaries into the interstitial fluid and across the cell membrane of individual cells. The individual cells then use the O_2 to produce ATP, which releases CO_2 as a by-product.
5. By the time blood has reached the venous end of a capillary network, it has achieved an equilibrium with the cells and interstitial fluid.

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PROCESS Figure

Inspired air
P_{O_2} = 160
P_{CO_2} = 0.3
Alveolus
P_{CO_2} = 40 P_{O_2} = 104
1 At the alveoli, O_2 diffuses into and CO_2 diffuses out of the blood
P_{CO_2} = 45
P_{O_2} = 40
7% Dissolved in plasma
23% Bound to hemoglobin
93% Into red blood cells
70% Converted to HCO_3^-
CO_2 travels in the plasma in three ways
Right
5 Once at equilibrium, the gases stop diffusing (Go back to step 1)
P_{O_2} = 40
P_{CO_2} = 45
P_{O_2} = 40
P_{CO_2} = 45
Expired air
P_{O_2} = 120
P_{CO_2} = 27
Alveolus
P_{O_2} = 104 P_{CO_2} = 40
2 Once at equilibrium, the gases stop diffusing
P_{O_2} = 104
P_{CO_2} = 40
Pulmonary capillary
P_{O_2} = 95
P_{CO_2} = 40
3 Blood in pulmonary veins
O_2 travels in the plasma bound to hemoglobin molecules in the cytoplasm of red blood cells. Each hemoglobin molecule can carry 4 O_2 molecules.
Left
Heart

PROCESS Figure 15.13 APR **Gas Exchange**

Differences in partial pressure are responsible for the exchange of O_2 and CO_2 that occurs between the alveoli and the pulmonary capillaries and between the tissues and the tissue capillaries.

Understand **What effect would breathing into and out of a paper bag have on CO_2 diffusion at the alveoli?**

Carbon Dioxide Partial Pressure Gradients

The partial pressure gradient for CO_2 is the opposite that for O_2. Carbon dioxide moves out of the body's cells and into the blood. Once in the blood, the partial pressure gradient for CO_2 is out of the blood into the alveoli.

We will now follow the process in *reverse order* in figure 15.13 as it describes the specific partial pressures for CO_2 as it moves away from the body's cells toward the alveoli.

1. As cells produce CO_2, the intracellular Pco_2 increases to approximately 46 mm Hg and the interstitial fluid Pco_2 is approximately 45 mm Hg. The Pco_2 of arterial blood as it arrives in the tissues is 40 mm Hg. Thus, CO_2 diffuses out of the cells, into the interstitial fluid and into the blood, down its partial pressure gradient. By the time blood has reached the venous end of the capillary network, it has achieved an equilibrium with the interstitial fluid and has a Pco_2 of 45 mm Hg.
2. The Pco_2 of the blood when it returns to the arterial end of the pulmonary capillaries is still 45 mm Hg compared to a Pco_2 of 40 mm Hg in the alveoli. Thus, at the alveoli, CO_2 diffuses out of the blood down its partial pressure gradient. At the venous end of the pulmonary capillaries, Pco_2 has achieved an equilibrium with the alveoli and has decreased to 40 mm Hg.

Respiratory Membrane Thickness

Increasing the thickness of the respiratory membrane decreases the rate of gas diffusion. The thickness of the respiratory membrane can be increased by certain diseases. A two- or three-fold thickness increase markedly decreases the rate of gas exchange. The most common cause of increased respiratory membrane thickness is an accumulation of fluid in the alveoli, known as *pulmonary edema*. Alveolar fluid accumulation is usually caused by failure of the left side of the heart. Left-side heart failure increases venous pressure in the pulmonary capillaries and causes fluid to accumulate in the alveoli. Conditions that result in inflammation of the lung tissues, such as with tuberculosis or pneumonia, can also cause fluid accumulation within the alveoli.

Respiratory Membrane Surface Area

In a healthy adult, the total surface area of the respiratory membrane is approximately 70 m^2 (approximately one-fourth of the size of a tennis court or the floor area of a 25- × 30-foot room). Several respiratory diseases, including emphysema and lung cancer, cause a decrease in the surface area of the respiratory membrane. Even small decreases in this surface area adversely affect the respiratory exchange of gases during strenuous exercise. When the total surface area of the respiratory membrane is decreased to one-third or one-fourth of normal, the exchange of gases is significantly restricted, even under resting conditions.

A decreased surface area for gas exchange can also result from the surgical removal of lung tissue, the destruction of lung tissue by cancer, the degeneration of the alveolar walls by emphysema, or the replacement of lung tissue by connective tissue due to tuberculosis. More acute conditions that cause the alveoli to fill with fluid also reduce the surface area for gas exchange because the increased thickness of the respiratory membrane caused by the fluid accumulation makes the alveoli nonfunctional. This may occur in pneumonia or in pulmonary edema resulting from failure of the left ventricle.

15.6 OXYGEN AND CARBON DIOXIDE TRANSPORT IN THE BLOOD

Learning Outcomes *After reading this section, you should be able to*

A. Contrast sickle-cell hemoglobin with non-sickle-cell hemoglobin.
B. Explain how O_2 and CO_2 are transported in the blood.
C. Explain the CO_2 exchange in the lungs and at the tissues.
D. Discuss the factors that affect O_2 and CO_2 transport in the blood.

Once O_2 and CO_2 enter the blood, they each interact with components there that aid in their solubility and reduce the potentially dangerous impact CO_2 could have on blood pH. Both O_2 and CO_2 are transported by the protein, hemoglobin; however, CO_2 is also transported in other ways.

Hemoglobin

Hemoglobin is a complex protein synthesized by immature red blood cells. Recall from chapter 11 that hemoglobin remains within the cytoplasm of red blood cells and occupies about one-third of their total volume.

Hemoglobin consists of four subunits, each containing one iron-based heme group. It is the heme group to which O_2 binds, so one hemoglobin can carry up to four O_2 molecules.

An altered form of hemoglobin can be found in individuals with sickle-cell disease. Under low O_2 conditions, this type of hemoglobin molecule binds to other sickle-cell hemoglobin molecules inside red blood cells. The binding together of the sickle-cell hemoglobin molecules causes the red blood cells to become sickle-shaped. The sickle-shaped red blood cells become lodged inside small capillaries and block blood flow.

Transport of O_2

Once O_2 diffuses through the respiratory membrane into the blood, it is transported to all the cells of the body. Approximately 98.5% of O_2 is transported reversibly bound to hemoglobin within red blood cells, and the remaining 1.5% is dissolved in the plasma. Cells use O_2 in aerobic respiration to synthesize ATP (see chapter 17).

Transport of CO_2

Carbon dioxide is formed as a by-product of the breakdown of glucose when cells use O_2 to produce ATP. The CO_2 diffuses out of individual cells into the blood. The blood concentration of CO_2 needs to be very tightly regulated because too much CO_2 in the blood causes the blood to become acidic.

There are three ways CO_2 is transported in the blood: (1) dissolved in the plasma, (2) bound to hemoglobin, and (3) converted to bicarbonate ion (HCO_3^-) (figure 15.14).

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Figure 15.14 **Transport of CO_2**

Carbon dioxide is transported in three different ways in the blood: (1) a small portion dissolves directly in the plasma, (2) some binds to the globin portion of hemoglobin in the cytoplasm of red blood cells, and (3) the majority is converted by carbonic anhydrase to bicarbonate ion in the cytoplasm of red blood cells. The bicarbonate ions are transported out of the red blood cells and into the plasma.

Transport of CO_2 in the Plasma

About 7% of CO_2 dissolves directly in the plasma as it diffuses out of the cells and into the blood. The remaining CO_2 diffuses into the red blood cells where it either binds to hemoglobin or is converted to HCO_3^-.

Transport of CO_2 by Hemoglobin

Approximately 23% of CO_2 is transported bound to hemoglobin (see figure 15.14). Many CO_2 molecules bind in a reversible fashion to the protein chains of hemoglobin molecules. Carbon dioxide's ability to bind to hemoglobin is affected by the amount of O_2 bound to hemoglobin. The smaller the amount of O_2 bound to hemoglobin, the greater the amount of CO_2 able to bind to it, and vice versa. In tissues, as hemoglobin binds CO_2, the affinity of hemoglobin for O_2 is reduced. This is beneficial because tissues with higher levels of CO_2 demand more O_2 in order to continue aerobic respiration, our cells' most efficient means of producing ATP.

Transport of CO_2 as Bicarbonate Ions

About 70% of blood CO_2 is transported in the form of HCO_3^-, dissolved in either the cytoplasm of red blood cells or the plasma of the blood. Within red blood cells, an enzyme called **carbonic anhydrase** catalyzes a reversible reaction (see chapter 2). Carbonic anhydrase catalyzes the production of carbonic acid (H_2CO_3) from CO_2 and H_2O. The H_2CO_3 then dissociates into H^+ and HCO_3^- shown by the following equation:

$$\underset{\text{Carbon dioxide}}{CO_2} + \underset{\text{Water}}{H_2O} \overset{\text{Carbonic anhydrase}}{\rightleftarrows} \underset{\text{Carbonic acid}}{H_2CO_3} \rightleftarrows \underset{\text{Hydrogen ion}}{H^+} + \underset{\text{Bicarbonate ion}}{HCO_3^-}$$

As CO_2 levels increase, more H^+ is produced. Recall from chapter 2 that higher concentrations of H^+ cause the pH to decrease and the solution becomes acidic. However, because this is a reversible reaction, if CO_2 levels decrease, carbonic anhydrase creates H_2CO_3 upon the combining of H^+ and HCO_3^-. The H_2CO_3 then dissociates to form CO_2 and H_2O, which lowers H^+ concentration and pH increases into a more basic (alkaline) range.

At the tissues, where CO_2 levels are higher, HCO_3^- is removed from the red blood cell by an HCO_3^-/Cl^- antiporter. In the tissues, HCO_3^- diffuses out of the red blood cell while Cl^- diffuses in through the antiporter. This exchange maintains electrical neutrality in the red blood cells and plasma.

Summary of Gas Transport

Figure 15.15 summarizes the event in the transport of both O_2 from the lungs to the tissues and CO_2 from the tissues to the lungs. Figure 15.15*a* summarizes the events as O_2 enters the blood from the alveoli and CO_2 exits the blood.

PROCESS Figure

PROCESS Figure 15.15 APR **Gas Exchange in the Tissues and in the Lungs**

(*a*) In the tissues, CO_2 diffuses into red blood cells, where the enzyme carbonic anhydrase (CA) is located. CA catalyzes the reaction of CO_2 with H_2O to form carbonic acid (H_2CO_3). H_2CO_3 dissociates to form bicarbonate ions (HCO_3^-) and hydrogen ions (H^+). Oxygen is released from hemoglobin (Hb) and diffuses into tissue cells. (*b*) In the lungs, CO_2 diffuses from red blood cells into the alveoli. CA catalyzes the formation of CO_2 and H_2O from H_2CO_3. H^+ and HCO_3^- combine to replace H_2CO_3. Oxygen diffuses into red blood cells and binds to hemoglobin.

Apply **How would the cytoplasmic pH of red blood cells be affected by anemia that is caused by reduced hemoglobin levels?**

❶ In the lungs, carbon dioxide (CO_2) diffuses from red blood cells and plasma into the alveoli.

❷ Carbonic anhydrase catalyzes the formation of CO_2 and H_2O from H_2CO_3.

❸ Bicarbonate ions and H^+ combine to replace H_2CO_3.

❹ In the chloride shift, a membrane transport protein allows HCO_3^- to diffuse into the red blood cells and chloride ions (Cl^-) to diffuse out of them, which maintains their electrical neutrality.

❺ Oxygen diffuses into the plasma and into red blood cells. Some of the O_2 remains in the plasma. Oxygen binds to hemoglobin.

❻ Hydrogen ions are released from hemoglobin, which promotes the uptake of O_2 by hemoglobin.

❼ Carbon dioxide is released from hemoglobin. Hemoglobin that is bound to O_2 readily releases CO_2.

Figure 15.15*b* summarizes the events as O_2 is delivered to the tissues and CO_2 is transported away from the tissues.

❶ In the tissues, carbon dioxide (CO_2) diffuses into the plasma and into red blood cells. Some of the carbon dioxide remains in the plasma.

❷ In red blood cells, carbon dioxide reacts with water (H_2O) to form carbonic acid (H_2CO_3) in a reaction catalyzed by the enzyme carbonic anhydrase (CA).

❸ Carbonic acid dissociates to form bicarbonate ions (HCO_3^-) and hydrogen ions (H^+).

❹ In the chloride shift, a membrane transporter allows HCO_3^- to diffuse out of the red blood cells and chloride ions (Cl^-) to diffuse into them, which maintains their electrical neutrality.

❺ Oxygen (O_2) is released from hemoglobin (Hb). Oxygen diffuses out of red blood cells and plasma into the tissue.

❻ Hydrogen ions combine with hemoglobin, which promotes the release of oxygen from hemoglobin.

❼ Carbon dioxide combines with hemoglobin. Hemoglobin that has released oxygen readily combines with carbon dioxide. $HCO_3^- + H^+$.

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There are many physiological factors that modulate the affinity of hemoglobin for both O_2 and CO_2. For example, under conditions of increased O_2 demand, the affinity of hemoglobin for O_2 is reduced. A discussion of some of these conditions follows.

Physiological Factors Affecting Gas Transport

The respiratory system maintains blood O_2 and CO_2 concentrations and blood pH within normal values. Changes in these levels out of their normal range have a noticeable influence on the relationship between hemoglobin, O_2, and CO_2. **Chemoreceptors** are specialized neurons that detect changes in the concentration of specific chemicals. The chemoreceptors involved in regulating respiration respond to changes in pH, changes in Po_2, Pco_2, or all three.

Effect of Po_2 on O_2 Transport

The relationship between O_2 and hemoglobin is similar to that of a ligand and its receptor in that hemoglobin has specific binding sites for O_2. These binding sites are the heme groups of the hemoglobin. Hemoglobin is 100% saturated with O_2 when four O_2 molecules are bound to each hemoglobin molecule in the red blood cells. When there is an average of two O_2 molecules bound to each hemoglobin molecule, hemoglobin is 50% saturated.

Apply It 4

In carbon monoxide (CO) poisoning, CO binds to hemoglobin, thereby decreasing the uptake of O_2 by hemoglobin. In addition, when CO binds to hemoglobin,

hemoglobin has a greater attraction for O_2. How does this change in attraction for O_2 affect the ability of tissues to get O_2? Explain.

Effect of Po_2 on CO_2 Transport

The largest effect of Po_2 on CO_2 transport is at low Po_2 levels. Recall that when Po_2 levels are low, the hemoglobin binds more CO_2. In turn, as more CO_2 binds to hemoglobin, the affinity of hemoglobin for O_2 decreases.

Effect of pH and Pco_2 on O_2 Transport

In addition to Po_2, other factors, such as blood pH and Pco_2, influence the saturation of hemoglobin. As the pH of the blood drops (due to higher H^+ levels), the affinity of hemoglobin for O_2 at any given Po_2 is much lower. The higher H^+ levels bind to nonheme portions of hemoglobin, which changes its overall shape. Following the concept of form following function, changing the shape of hemoglobin would change its affinity for O_2. Conversely, an increase in blood pH results in an increased affinity of hemoglobin for O_2. An increase in Pco_2 also decreases hemoglobin's ability to bind O_2 due to the effect of CO_2 on pH. In addition, CO_2 can directly affect hemoglobin's ability to bind O_2. When CO_2 binds to the protein portion of hemoglobin (see chapter 11), hemoglobin's affinity for O_2 is reduced. These effects are beneficial to tissues when they are in high demand for O_2.

Apply It 5

How does the movement of CO_2 from fetal blood into maternal blood increase the movement of O_2 from maternal blood into fetal blood? (Hint: Consider the changes in affinity of hemoglobin for O_2.)

Effect of pH and Pco_2 on CO_2 Transport

The principal effect of pH and Pco_2 is on the affinity of hemoglobin for O_2. However, a higher Pco_2 results in a larger decrease in pH. The decrease in pH triggers an increased respiratory rate as we will discuss in section 15.7. The sensitivity to CO_2 is valuable for maintaining appropriate blood pH levels. Hold a contest with yourself or a friend: First, start the contest by timing how long each of you can hold your breath. Wait a few minutes. Then, mildly hyperventilate by exhaling 4-5 times in a row (being careful you don't pass out!), and then once again time how long you can hold your breath. Did you hold it longer this second time or the first time? Theoretically, should you be able to hold your breath longer the first time or the second time?

Apply It 6

Explain the effect of (1) hyperventilation and (2) holding one's breath on blood pH.

Effect of Temperature on O_2 Transport

An increase in temperature also decreases O_2's tendency to remain bound to hemoglobin. Therefore, elevated temperatures resulting from increased metabolism increase the amount of O_2 released into the tissues by hemoglobin. In less metabolically active tissues in which the temperature is lower, less O_2 is released from hemoglobin.

Effect of Temperature on CO_2 Transport

Typically, when body temperature increases, the rate of ATP production is increased. Thus, more CO_2 enters the blood and eventually is converted into H^+ and HCO_3^-, lowering the pH. As we

discussed, the response is often an increased respiratory rate, which removes excess CO_2 from the body.

Effect of Glucose Metabolism on O_2 Transport

As red blood cells metabolize glucose for energy, they produce a by-product that reduces hemoglobin's affinity for O_2. Thus, hemoglobin releases more O_2. When blood is removed from the body and stored in a blood bank, the levels of this by-product in the stored blood decrease and blood becomes unsuitable for transfusion after approximately 6 weeks. Banked blood is, therefore, discarded after 6 weeks of storage.

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CLINICAL IMPACT

Effects of High Altitude and Emphysema

Air is composed of 21% O_2 at both low and high altitudes. At sea level, the atmospheric pressure is 760 mm Hg, and Po_2 is about 160 mm Hg (760 mm Hg × 0.21 = 160 mm Hg). At higher altitudes, the atmospheric pressure is lower, and Po_2 is decreased. For example, at 10,000 ft above sea level, the atmospheric pressure is 523 mm Hg. Consequently, Po_2 is 110 mm Hg (523 mm Hg × 0.21 = 110 mm Hg). Because Po_2 is lower at high altitudes, the blood levels of O_2 can decline enough to stimulate the carotid and aortic bodies. Oxygen then becomes an important stimulus for elevating the rate and depth of breathing. At high altitudes, the respiratory system's ability to eliminate CO_2 is not adversely affected by the low atmospheric pressure. Thus, the blood CO_2 levels become lower than normal because of the increased rate and depth of breathing stimulated by the low blood O_2 levels. The decreased blood CO_2 levels cause the blood pH to become abnormally high.

A similar situation can exist in people with emphysema; the destruction of the respiratory membrane allows less O_2 to move into the blood. The resulting low arterial Po_2 levels stimulate an increased rate and depth of respiration. At first, arterial Pco_2 levels may be unaffected by the reduced surface area of the respiratory membrane, because CO_2 diffuses across the respiratory membrane 20 times more readily than does O_2. However, if alveolar ventilation increases to the point that CO_2 exchange increases above normal, arterial CO_2 becomes lower than normal. More severe emphysema, in which the respiratory membrane surface area is reduced to a minimum, can decrease CO_2 exchange to the point that arterial CO_2 becomes elevated.

Apply It 7

If a person lacks the enzymes necessary for glucose metabolism inside red blood cells, does he or she exhibit anemia (a lower-than-normal number of red blood cells) or erythrocytosis (a higher-than-normal number of red blood cells)? Explain.

15.7 REGULATION OF VENTILATION

Learning Outcomes *After reading this section, you should be able to*

A. Describe the respiratory areas of the brainstem and how they produce a rhythmic pattern of ventilation.
B. Explain how blood pH, CO_2, and O_2 levels affect ventilation.
C. Discuss the Hering-Breuer reflex and its importance.
D. Explain how the cerebral cortex and limbic system can affect ventilation.

There are many factors that regulate respiratory rate. The body is particularly sensitive to changes in CO_2 levels and blood pH.

The medulla oblongata controls the respiratory rate. Neurons there control the basic rhythm of ventilation through stimulation of the muscles of respiration. The recruitment of muscle fibers and the more frequent stimulation of muscle fibers result in stronger muscle contractions and increased depth of respiration. The rate of respiration is determined by how frequently the respiratory muscles are stimulated.

Respiratory Areas in the Brainstem

Neurons involved with respiration are aggregated in certain parts of the brainstem. Scientists have learned that neurons that are active during inspiration are intermingled with those that are active during expiration.

The **medullary respiratory center** in the medulla oblongata consists of two sets of neurons: (1) the dorsal respiratory group and (2) the ventral respiratory group. The **dorsal respiratory group** forms a longitudinal column of cells in the dorsal part of each half of the medulla oblongata. The **ventral respiratory group** forms a longitudinal column of cells located in the ventral part of each half of the medulla oblongata (figure 15.16). Communication occurs between the two halves of the medulla within a respiratory group, so that respiratory movements are symmetrical. Communication also occurs between the dorsal and ventral respiratory groups.

Figure 15.16 **Respiratory Structures in the Brainstem**

Specific structures in the brainstem correlate with the nerves that innervate the muscles of respiration.

The dorsal respiratory group is a collection of neurons that are most active during inspiration, and stimulate contraction of the diaphragm. The ventral respiratory group is a collection of neurons that are active during both inspiration and expiration. A part of the ventral respiratory group, the **pre-Bötzinger complex,** is believed to establish the basic rhythm of respiration.

The **pontine respiratory group,** formerly called the pneumo-taxic center, is a collection of neurons in the pons that helps regulate respiration rate (figure 15.16). Some of the neurons are active only during inspiration, some only during expiration, and others during both inspiration and expiration. The precise function of the pontine respiratory group is unknown, but it has connections with the medullary respiratory center and appears to play a role in switching between inspiration and expiration, thus fine-tuning the breathing pattern. It is not considered essential for the generation of the respiratory rhythm.

Generation of Rhythmic Ventilation

One explanation for the generation of rhythmic ventilation involves the integration of a series of stimuli that start and stop inspiration:

1. *Starting inspiration*. Neurons in the medullary respiratory center spontaneously establish the basic rhythm of ventilation. The medullary respiratory center constantly receives stimulation from receptors that monitor blood gas levels, blood temperature, and the movements of muscles and joints. In addition, stimulation from the parts of the brain concerned with voluntary respiratory movements and emotions can occur. Inspiration starts when the combined input from all these sources causes the production of action potentials in the neurons that stimulate respiratory muscles.
2. *Increasing inspiration*. Once inspiration begins, more and more neurons are gradually activated. The result is progressively stronger stimulation of the respiratory muscles, which lasts for approximately 2 seconds.
3. *Stopping inspiration*. The neurons stimulating the muscles of respiration also stimulate the neurons in the medullary respiratory center that are responsible for stopping inspiration. The neurons responsible for stopping inspiration also receive input from the pontine respiratory group, stretch receptors in the lungs, and probably other sources. When these inhibitory neurons are activated, they inhibit the neurons that stimulate respiratory muscles. Relaxation of respiratory muscles results in expiration, which lasts approximately 3 seconds. The next inspiration begins again at step 1, *Starting inspiration.*

Although the medullary neurons establish the basic rate and depth of ventilation, their activities can be influenced by input from other parts of the brain and by input from peripherally located receptors.

Effect of Po_2 on Respiratory Rate

Carbon dioxide is the principal regulator of respiratory rate. However, changes in Po_2 can also affect respiration (figure 15.17; 15.18). A decrease in O_2 below its normal values is called **hypoxia** (high-POK-see-ah). If Po_2 levels in the arterial blood are markedly reduced while the pH and Pco_2 are held constant, an increase in ventilation rate occurs. However, within a normal range of Po_2 levels, the effect of O_2 on the regulation of respiration is small. Only after arterial Po_2 decreases to approximately 50% of its normal value does it begin to have a large stimulatory effect on respiratory movements. If Po_2 decreases sufficiently, the respiratory center can fail, resulting in death.

Homeostasis Figure 15.17 **Regulation of Blood pH**

(1) Blood pH is in its normal range. (2) Blood pH increases outside its normal range, which disturbs homeostasis. (3) The control centers for blood pH, the medullary chemoreceptors, detect an increase in blood pH (blood becomes more basic) and respond to the increased pH by signaling a decreased breathing rate. (4) The effectors, the diaphragm and other respiratory muscles, respond by slowing their contraction rate, which lowers the rate of breathing. (5) As a result, more CO_2 is retained, which causes pH to drop (blood becomes more acidic). (6) Blood pH returns to its normal range and homeostasis is maintained. Observe the responses to a decrease in blood pH by following the lower, red arrows.

Figure 15.18 **Nervous and Chemical Mechanisms of Breathing**

Several regulatory mechanisms affect the rate and depth of breathing. A plus sign indicates that the mechanism increases breathing and a minus sign indicates that it results in a decrease in breathing.

Understand

Apply It 8

Even people in "good shape" will have trouble breathing at high altitudes. Explain how this can happen, even when ventilation of the lungs increases.

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Effect of Pco_2 on Respiratory Rate

Blood CO_2 levels are a major regulator of respiration during both resting conditions and intense exercise. Even a small increase in CO_2 in the bloodstream triggers a large increase in the rate and depth of ventilation. For example, an increase in Pco_2 of only 5 mm Hg causes an increase in ventilation of 100%. A greater-than-normal amount of CO_2 in the blood is called **hypercapnia** (HIGH-per-KAP-nee-ah) and a lower than normal CO_2 level is called **hypocapnia** (HIGH-poh-KAP-nee-ah). Hypocapnia results in periods when the breathing rate is reduced or does not occur at all.

The chemoreceptors in the chemosensitive area of the medulla oblongata and in blood vessels near the heart respond to changes in CO_2 primarily because of the effects of CO_2 on blood pH (figure 15.17). The chemosensitive area in the medulla oblongata is far more important in regulating Pco_2 and pH than either the carotid or the aortic bodies. The carotid and aortic bodies are responsible for, at most, 15–20% of the total response to changes in Pco_2 or pH. During intense exercise, however, the carotid bodies respond more rapidly to changes in blood pH than does the chemosensitive area of the medulla.

Effect of pH on Respiratory Rate

The central chemoreceptors in the medulla oblongata detect changes in blood pH due to changes in CO_2. The carotid and aortic bodies detect changes in pH due to changes in H^+ concentrations. Because H^+ does not easily cross the blood-brain barrier or the blood-cerebrospinal fluid barrier (see chapter 8), the central chemoreceptors detect changes in blood pH through changes in blood CO_2. Carbon dioxide easily diffuses across the blood-brain barrier and the blood-cerebrospinal fluid barrier. The lower pH then stimulates the respiratory center, resulting in a greater rate and depth of breathing reducing CO_2 levels, and blood pH increases to normal levels.

Maintaining body pH levels within normal limits is necessary for the proper functioning of cells. Because changes in CO_2 levels can change pH, the respiratory system plays an important role in acid-base balance. The respiratory system's role in maintaining pH is considered in greater detail in chapter 18.

The Hering-Breuer Reflex and Respiratory Rate

The Hering-Breuer (HER-ing BROY-er) reflex limits the depth of inspiration and prevents overinflation of the lungs (see figure 15.18*d*). This reflex depends on stretch receptors in the walls of the bronchi and bronchioles of the lungs. Action potentials are initiated in these stretch receptors when the lungs are inflated and are passed along sensory neurons to the medulla oblongata. The action potentials have an inhibitory influence on the respiratory center and result in expiration. As expiration proceeds, the stretch receptors are no longer stimulated, and the decreased inhibitory effect on the respiratory center allows inspiration to begin again.

In infants, the Hering-Breuer reflex plays a role in regulating the basic rhythm of breathing and in preventing overinflation of the lungs. In adults, however, the reflex is important only when the tidal volume is large, such as during exercise.

Cerebral and Limbic System Control of Respiratory Rate

The rate and depth of breathing is controlled both voluntarily and involuntarily by the cerebral cortex (see figure 15.18). For example, during talking or singing, air movement is controlled to produce sounds, as well as to facilitate gas exchange.

During exercise, respiratory rate changes are controlled through various inputs to the respiratory center. Initially, there is a very rapid increase that occurs too quickly to be accounted for by changes in metabolism. For example, movement of the limbs has a strong stimulatory influence on the respiratory center (figure 15.18*e*). After the initial immediate increase in respiratory rate, there is a gradual increase that levels off within 4–6 minutes. The highest level of exercise that can be performed without causing a significant change in blood pH is called the **anaerobic threshold.** If the exercise intensity is high enough to exceed the anaerobic threshold, blood pH drops. The drop in pH stimulates the carotid bodies, which increases ventilation. In fact, ventilation can increase so much that arterial Pco_2 decreases below resting levels and arterial Po_2 increases above resting levels. In response to training, athletic performance increases because the cardiovascular and respiratory systems become more efficient at delivering O_2 and picking up CO_2. Ventilation does not limit performance in most individuals because ventilation can increase to a greater extent than does cardiovascular function. In conditioned athletes, the respiratory rate at rest or during submaximal exercise is slightly lower than in a non-athlete. However, athletes have higher respiratory rates at maximal exercise.

Emotions acting through the limbic system of the brain can also affect the respiratory center (see figure 15.18*a*). For example, strong emotions can cause hyperventilation or produce the sobs and gasps of crying.

Other Modifications of Ventilation

Higher brain centers control the respiratory system when touch, thermal, or pain receptors are activated (see figure 15.18*f*). For example, irritants in the nasal cavity can initiate a sneeze reflex, and irritants in the lungs can stimulate a cough reflex. An increase in body temperature can stimulate increased ventilation because metabolism is elevated and more CO_2 is produced, which then needs to be expelled from the body.

Understand

Apply It 9

Suppose that cold water is suddenly splashed on you. Describe your respiratory response. In the past, newborn babies were sometimes swatted on the buttocks. Explain the rationale for this procedure.

EFFECTS OF AGING ON THE RESPIRATORY SYSTEM

Most aspects of the respiratory system are affected by aging. However, even though vital capacity, maximum ventilation rates, and gas exchange decrease with age, the elderly can engage in light to moderate exercise because the respiratory system has a large reserve capacity.

Vital capacity decreases with age because of a decreased ability to fill the lungs (decreased inspiratory reserve volume) and a decreased ability to empty the lungs (decreased expiratory reserve volume). As a result, maximum minute volume rates decrease, which in turn decreases the ability to perform intense exercise. These changes are related to weakening of respiratory muscles and to decreased compliance of the thoracic cage caused by the stiffening of cartilage and ribs. Lung compliance actually increases with age, but this effect is offset by the decreased thoracic cage compliance. Lung compliance increases because parts of the alveolar walls are lost, which reduces lung recoil. No significant age-related changes take place in lung elastic fibers or surfactant.

Alveolar ducts and many of the larger bronchioles expand in diameter with age, which increases residual volume. Larger bronchioles and alveolar ducts create more dead space, lowering the amount of air available for gas exchange (alveolar ventilation). In addition, gas exchange across the respiratory membrane is reduced because parts of the alveolar walls are lost, which decreases the surface area available for gas exchange, and the remaining walls thicken, which decreases the diffusion of gases. A gradual rise in resting tidal volume with age compensates for these changes.

With age, mucus accumulates within the respiratory passageways because it becomes more viscous and because the number of cilia and their rate of movement decrease. As a consequence, the elderly are more susceptible to respiratory infections and bronchitis.

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SYSTEMS PATHOLOGY

Asthma

Background Information

Will has asthma. **Asthma** (AZ-mah; difficult breathing) is characterized by abnormally increased constriction of the trachea and bronchi in response to various stimuli, which decrease ventilation efficiency (figure 15.19). Symptoms include rapid and shallow breathing, wheezing, coughing, and shortness of breath (figure 15.20). In contrast to many other respiratory disorders, the symptoms of asthma typically reverse either spontaneously or with therapy.

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Figure 15.19 Effects of Asthma on Other Body Organ Systems
There are many factors that can induce an asthma attack.

Figure 15.20 Effect of Asthma on Ease of Breathing and Air Passages

Strenuous exercise is one of the many factors that can bring on an asthma attack.

(a) Chris Cole/The Image Bank/Getty Images; (b) (*left*) Carolina Biological/Medical Images; (*right*) Image Source/Getty Images

There is no definitive pathological feature or diagnostic test for asthma, but three important characteristics of the disease are chronic airway inflammation, airway hyperreactivity, and airflow obstruction. The inflammation can block airflow through the bronchi. Airway hyperreactivity means that the smooth muscle in the trachea and bronchi contracts greatly in response to a stimulus, thus decreasing the diameter of the airway and increasing resistance to airflow. The effects of inflammation and airway hyperreactivity combine to cause airflow obstruction (figure 15.20).

Many cases of asthma appear to be associated with a chronic inflammatory response by the immune system. Inflammation appears to be linked to airway hyperreactivity by some chemical mediators released by immune cells.

The stimuli that prompt airflow obstruction in asthma vary from one individual to another. Some asthmatics react to particular allergens, which are foreign substances that evoke an inappropriate immune system response (see chapter 14). Examples include inhaled pollen, animal dander, dust mites, and droppings and carcasses of cockroaches. However, other inhaled substances, such as chemicals in the workplace or cigarette smoke, can provoke an asthma attack without stimulating an allergic reaction. An asthma attack can also be stimulated by ingested substances such as some medicines.

Other stimuli, such as strenuous exercise (especially in cold weather) can precipitate an asthma attack. Such episodes can often be avoided by using a bronchodilator prior to exercise. Viral infections, emotional upset, stress, air pollution, and even reflux of stomach acid into the esophagus are known to elicit asthma attacks.

Treatment of asthma involves avoiding the causative stimulus and taking medications. Steroids and mast cell–stabilizing agents, which prevent the release of chemical mediators from mast cells, can reduce airway inflammation. Bronchodilators are used to increase airflow. Table 15.2 describes several other diseases and disorders of the respiratory system that can occur during any stage of life.

TABLE 15.2 REPRESENTATIVE DISEASES AND DISORDERS: Respiratory System

Condition	Description
RESPIRATORY DISORDERS	
Bronchitis (brong-KIGH-tis)	Inflammation of bronchi impairs breathing; bronchitis can progress to emphysema
Emphysema (em-fih-SEE-mah)	Destruction of alveolar walls; loss of alveoli decreases surface area for gas exchange; there is no cure; alone or with bronchitis, known as **chronic obstructive pulmonary disease (COPD)**
Adult respiratory distress syndrome (ARDS)	Caused by damage to the respiratory membrane; amount of surfactant is reduced lessening gas exchange; develops after an injurious event
Cystic fibrosis (figh-BROH-sis)	Genetic disorder that affects mucus secretions throughout the body due to an abnormal transport protein; mucus is much more viscous and accumulates in ducts and tubes, such as the bronchioles; airflow is restricted, and infections are more likely
Lung cancer	Occurs in the epithelium of the respiratory tract; can easily spread to other parts of the body because of the rich blood and lymphatic supply to the lungs
Circulatory System	
Thrombosis of the pulmonary arteries	Blood clot in lung blood vessels; inadequate blood flow through the pulmonary capillaries, affecting respiratory function
Nervous System	

Condition	Description
Sudden infant death syndrome (SIDS)	Most frequent cause of death of infants between 2 weeks and 1 year of age; cause is still unknown, but at-risk babies can be placed on monitors that warn if breathing stops
INFECTIOUS DISEASES OF THE RESPIRATORY SYSTEM	
Upper Respiratory Tract	
Strep throat	Caused by streptococcal bacteria (*Streptococcus pyogenes*); characterized by inflammation of the pharynx and fever
Common cold	Results from a viral infection
Lower Respiratory Tract	
Tuberculosis (too-BER-kyoo-LOH-sis)	Caused by the bacterium *Clostridium tuberculosis,* which forms small, lumplike lesions called tubercles
Pneumonia (noo-MOH-nee-ah)	Many bacterial or viral infections of the lungs that cause fever, difficulty in breathing, and chest pain; edema in the lungs reduces their inflation ability and reduces gas exchange
Flu (influenza; in-floo-EN-zah)	Viral infection of the respiratory system; does not affect the digestive system, as is commonly misunderstood

Apply It 10

It is not usually necessary to assess arterial blood gases when diagnosing and treating asthma. However, this information can sometimes be useful in severe asthma attacks. Suppose that Will had a Po_2 of 60 mm Hg and a Pco_2 of 30 mm Hg when he first went to the emergency room. Explain how that could happen.

SUMMARY

15.1 Anatomy of the Respiratory System

The respiratory system structures start with the nose and end with the alveoli in the lungs.

15.2 Functions of the Respiratory System

1. Respiration includes the movement of air into and out of the lungs, the exchange of gases between the air and the blood, the transport of gases in the blood, and the exchange of gases between the blood and tissues.
2. Other functions of the respiratory system are regulation of blood pH, production of chemical mediators, voice production, olfaction, and protection against some microorganisms.

15.3 Structures and Histology of the Respiratory Tract

The Upper Respiratory Tract

Nose and Nasal Cavity

1. The nose consists of the external nose and the nasal cavity.
2. The bridge of the nose is bone, and most of the external nose is cartilage.
3. Openings of the nasal cavity
   - The nares open to the outside, and then to the pharynx.
   - The paranasal sinuses and the nasolacrimal duct open into the nasal cavity.
4. Parts of the nasal cavity
   - The nasal cavity is divided by the nasal septum.
   - The nasal cavity is lined with pseudostratified ciliated columnar epithelium that traps debris and moves it to the pharynx.
   - The superior part of the nasal cavity contains the olfactory epithelium.
5. The nasal cavity serves as a passageway for air; cleans and humidifies air; is the location for the sense of smell; and, with the paranasal sinuses, functions as a resonating chamber for speech.

Pharynx

1. The nasopharynx joins the nasal cavity through the internal choanae and contains the openings to the auditory tube and the pharyngeal tonsils.
2. The oropharynx joins the oral cavity and contains the palatine and lingual tonsils.
3. The laryngopharynx opens into the larynx and the esophagus.

Larynx

1. Three of the nine cartilages are single cartilages. The thyroid cartilage and cricoid cartilage form most of the larynx. The epiglottis covers the opening of the larynx during swallowing. Six of the cartilages are paired. The vocal folds attach to the arytenoid cartilages.
2. The larynx maintains an open air passageway, regulates the passage of swallowed materials and air, produces sounds, and removes debris from the air.
3. Sounds are produced as the vocal folds vibrate when air passes through the larynx.
   Tightening the folds produces sounds of different pitches by controlling the length of the fold, which is allowed to vibrate.

The Lower Respiratory Tract

Trachea

1. The trachea connects the larynx to the main bronchi.
2. Smooth muscle regulates the diameter of the trachea.

Bronchi

The trachea divides to form two main bronchi, which extend to the lungs.

Tracheobronchial Tree

1. The main bronchi divide to form lobar bronchi, which divide to form segmental bronchi, which divide to form bronchioles, which divide to form terminal bronchioles.
2. The trachea to the terminal bronchioles is a passageway for air movement.

- The area from the trachea to the terminal bronchioles is ciliated to facilitate the removal of inspired debris.
- Cartilage helps hold the tube system open (from the trachea to the bronchioles).
- Smooth muscle controls the diameter of the tubes (terminal bronchioles).

Alveoli

1. Terminal bronchioles divide to form respiratory bronchioles, which give rise to alveolar ducts. Air-filled chambers called alveoli open into the respiratory bronchioles and alveolar ducts. The alveolar ducts end as alveolar sacs, which are chambers that connect to two or more alveoli.
2. Gas exchange occurs between the respiratory bronchioles and the alveoli.
3. The components of the respiratory membrane are a film of water, the walls of the alveolus and the capillary, and an interstitial space.

Thoracic Wall and Muscles of Respiration

The thoracic wall consists of vertebrae, ribs, the sternum, and muscles that allow expansion of the thoracic cavity.

Lungs

1. The thoracic cavity contains two lungs.
2. The lungs are divided into lobes, bronchopulmonary segments, and lobules.
3. There are three lung lobes on the right and two lung lobes on the left.
4. Each lung lobe is further subdivided into bronchopulmonary segments.

Blood Supply to the Lungs

1. Deoxygenated blood is transported to the lungs through the pulmonary arteries, and oxygenated blood leaves through the pulmonary veins.
2. Oxygenated blood is mixed with a small amount of deoxygenated blood from the bronchi.

Lymphatic Supply to the Lungs

The superficial and deep lymphatic vessels drain lymph from the lungs.

Pleura

The pleural membranes surround the lungs and protect against friction.

15.4 Behavior of Gases

Behavior of Gases and Ventilation

Ventilation is the movement of air into and out of the lungs.

Muscles of Respiration

1. Contraction of the diaphragm increases thoracic volume.
2. Muscles can elevate the ribs and increase thoracic volume or depress the ribs and decrease thoracic volume.

The Relationship Between Pressure Gradients and Ventilation

1. Air moves from an area of higher pressure to an area of lower pressure.
2. Pressure is inversely related to volume.

Measurement of Lung Function

Pulmonary Volumes and Capacities

1. Four pulmonary volumes exist: tidal volume, inspiratory reserve volume, expiratory reserve volume, and residual volume.
2. Pulmonary capacities are the sum of two or more pulmonary volumes and include inspiratory capacity, functional residual capacity, vital capacity, and total lung capacity.

Alveolar Ventilation

Alveolar ventilation is how much air per minute enters the parts of the respiratory system where gas exchange takes place.

Factors Affecting Ventilation

1. Gender, age, body size, and physical fitness all affect the degree of ventilation.
2. Ventilation is typically reduced in certain disease states.

Behavior of Gases and Respiration

Partial Pressure

1. Partial pressure is the contribution of a gas to the total pressure of a mixture of gases.
2. Water vapor pressure is the partial pressure produced by water.
3. Atmospheric air, alveolar air, and expired air have different compositions.

Diffusion of Gases into and out of Liquids

The concentration of a dissolved gas in a liquid is determined by its pressure and by its solubility coefficient.

15.5 Physiology of the Respiratory System

Mechanisms of Alveolar Ventilation

Changes in thoracic volume cause changes in pleural pressure, resulting in changes in alveolar volume, intra-alveolar pressure, and airflow.

Factors Affecting Alveolar Ventilation

Lung Recoil

- Lung recoil results from elastic fibers and water surface tension.
- Surfactant reduces water surface tension.

Pleural Pressure

- A negative pleural pressure can cause the alveoli to expand.
- Pneumothorax is an opening between the pleural cavity and the air that causes a loss of pleural pressure.

Factors Affecting Diffusion Through the Respiratory Membrane

The respiratory membrane is thin and has a large surface area that facilitates gas exchange.

Partial Pressure Gradients

1. Oxygen moves from the alveoli (Po_2 = 104 mm Hg) into the blood (Po_2 = 40 mm Hg). Blood is almost completely saturated with O_2 when it leaves the capillary.
2. The Po_2 in the blood decreases (Po_2 = 95 mm Hg) when it mixes with deoxygenated blood.
3. Oxygen moves from the tissue capillaries (Po_2 = 95 mm Hg) into the tissues (Po_2 = 40 mm Hg).
4. Carbon dioxide moves from the tissues (Pco_2 = 45 mm Hg) into tissue capillaries (Pco_2 = 40 mm Hg).
5. Carbon dioxide moves from the pulmonary capillaries (Pco_2 = 45 mm Hg) into the alveoli (Pco_2 = 40 mm Hg).

Respiratory Membrane Thickness

The rate of diffusion of gases through the respiratory membrane depends on its thickness, the diffusion coefficient of the gas.

Respiratory Membrane Surface Area

The surface area of the membrane and the partial pressure of the gases in the alveoli and the blood affect the rate of gas diffusion.

15.6 Oxygen and Carbon Dioxide Transport in the Blood

Hemoglobin

1. Adult hemoglobin is fully saturated when four O_2 are bound to it.
2. Hemoglobin-S is found in individuals with sickle-cell disease.

Transport of O_2

Oxygen is transported by hemoglobin (98.5%) and is dissolved in plasma (1.5%).

Transport of CO_2

Transport of CO_2 in the Plasma

Carbon dioxide is transported dissolved in plasma (7%).

Transport of CO_2 by Hemoglobin

The smaller the amount of O_2 bound to hemoglobin, the greater the amount of CO_2 bound to it, and vice versa.

Transport of CO_2 as Bicarbonate Ions

In tissue capillaries, the following events occur:

- Carbon dioxide combines with water inside red blood cells to form carbonic acid, which dissociates to form HCO_3^-. Decreasing HCO_3^- concentrations promote CO_2 transport.
- Exchange of Cl^- for HCO_3^- occurs between plasma and red blood cells.
- Hydrogen ions binding to hemoglobin promote CO_2 transport, prevent a pH change in red blood cells.

Summary of Gas Transport

Affinity of hemoglobin for O_2 decreases as O_2 demand increases.

Physiological Factors Affecting Gas Transport

The affinity of hemoglobin for O_2 is altered by several parameters including pH, temperature, and CO_2 levels.

Effect of Po_2 on O_2 Transport

Hemoglobin is completely saturated when bound to four O_2.

Effect of Po_2 on CO_2 Transport

At low Po_2 levels, hemoglobin binds more CO_2.

Effect of pH and Pco_2 on O_2 Transport

1. Hemoglobin's ability to hold O_2 decreases with decreased pH or increased CO_2.
2. Hemoglobin's ability to hold O_2 increases with increased pH decreased CO_2, or decreased temperature.

Effect of pH and Pco_2 on CO_2 Transport

There is little effect of pH on CO_2 transport.

Effect of Temperature on O_2 Transport

An increase in temperature decreases the affinity of hemoglobin for O_2.

Effect of Temperature on CO_2 Transport

At higher body temperatures, more CO_2 is produced, which results in an increased respiratory rate.

Effect of Glucose Metabolism on O_2 Transport

Glucose metabolism increases hemoglobin's ability to release O_2.

15.7 Regulation of Ventilation

Respiratory Areas in the Brainstem

1. The medullary respiratory center consists of the dorsal and ventral respiratory groups.
   - The dorsal respiratory groups stimulate the diaphragm.
   - The ventral respiratory groups stimulate the intercostal and abdominal muscles.
2. The pontine respiratory group is involved with switching between inspiration and expiration.

Generation of Rhythmic Ventilation

1. Neurons in the medullary respiratory center establish the basic rhythm of ventilation.
2. When stimuli from receptors or other parts of the brain exceed a threshold level, inspiration begins.
3. As respiratory muscles are stimulated, neurons that stop inspiration are stimulated. When the stimulation of these neurons exceeds a threshold level, inspiration is inhibited.

Effect of Po_2 on Respiratory Rate

Oxygen levels in the blood affect ventilation when a 50% or greater decrease from normal exists. Decreased O_2 is detected by receptors in the carotid and aortic bodies, which then stimulate the respiratory center.

Effect of Pco_2 on Respiratory Rate

Carbon dioxide is the major regulator of ventilation. An increase in CO_2 or a decrease in pH can stimulate the chemosensitive area, causing a greater rate and depth of ventilation.

Effect of pH on Respiratory Rate

A low pH stimulates an increased respiratory rate, which expels excess CO_2. A lower level of CO_2 returns pH to normal levels.

The Hering-Breuer Reflex and Respiratory Rate

Stretch of the lungs during inspiration can inhibit the respiratory center and contribute to a cessation of inspiration.

Cerebral and Limbic System Control of Respiratory Rate

1. Ventilation can be voluntarily controlled and can be modified by emotions.
2. The respiratory centers are stimulated during exercise.
3. Chemosensitive mechanisms and learning fine-tune the effects produced during exercise.

Other Modifications of Ventilation

Touch, thermal, and pain sensations can modify ventilation.

REMEMBERING AND UNDERSTANDING

1. Define respiration.
2. What are the functions of the respiratory system?
3. Describe the structures of the nasal cavity and their functions.
4. Name the three parts of the pharynx. With what structures does each part communicate?
5. Name and give the functions of the three unpaired cartilages of the larynx.
6. What are the functions of the vestibular and vocal folds? How are sounds of different loudness and pitch produced?
7. Starting at the larynx, name in order all the tubes air passes through to reach an alveolus.
8. What is the function of the C-shaped cartilages in the trachea? What happens to the amount of cartilage in the tube system of the respiratory system as the tubes become smaller? Explain why breathing becomes more difficult during an asthma attack.
9. What is the function of the ciliated epithelium in the tracheobronchial tree?
10. Distinguish among the lungs, a lobe of the lung, and a bronchopulmonary segment.
11. List the components of the respiratory membrane.
12. Describe the pleurae of the lungs. What is their function?
13. Describe the lymphatic supply of the lungs. What is its function?
14. Explain how the muscles of inspiration and expiration change thoracic volume.
15. Describe the pressure changes that cause air to move into and out of the lungs. What causes these pressure changes?
16. Give two reasons the lungs tend to recoil. What two factors keep the lungs from collapsing?

17. Explain how changes in thoracic volume result in changes in pleural pressure, alveolar volume, alveolar pressure, and airflow during inspiration and expiration.
18. Define tidal volume, inspiratory reserve volume, expiratory reserve volume, and residual volume. Define vital capacity, total lung capacity, and forced expiratory vital capacity.
19. Describe the factors that affect the diffusion of gases across the respiratory membrane. Give some examples of diseases that decrease diffusion by altering these factors.
20. What is the partial pressure of a gas? Describe the diffusion of O_2 and CO_2 between the alveoli and the pulmonary capillaries and between the tissue capillaries and the tissues in terms of partial pressures.
21. List the ways in which blood transports O_2. What factors promote the release of O_2 in tissues?
22. List the ways in which blood transports CO_2.
23. How does the level of blood CO_2 affect blood pH? How can changes in ventilation affect blood pH?
24. Name the respiratory areas of the brainstem, and explain how rhythmic breathing is generated.
25. Describe how higher brain centers and the Hering-Breuer reflex can modify breathing.
26. Explain the role of blood pH, CO_2, and O_2 in modifying breathing.
27. How is breathing regulated during exercise?
28. What effect does exercise training have on the respiratory system?
29. Why do vital capacity, alveolar ventilation, and diffusion of gases across the respiratory membrane decrease with age? Why are the elderly more likely to develop respiratory infections and bronchitis?

CRITICAL THINKING

1. Cardiopulmonary resuscitation (CPR) has replaced former methods of sustaining ventilation. The back pressure/arm lift method is one such technique that is no longer used. This procedure must be performed with the victim lying face down. The rescuer presses firmly on the base of the scapulae for several seconds, then grasps the arms and lifts them. The sequence is then repeated. Although this procedure is less efficient than CPR, it does result in ventilation of the lungs. Explain why.
2. Another technique for artificial respiration is mouth-to-mouth resuscitation. The rescuer takes a deep breath, blows air into the victim's mouth, and then lets air flow out of the victim's lungs. The process is repeated. Explain the following:
   a. Why do the victim's lungs expand?
   b. Why does air move out of the victim's lungs?
3. A person's vital capacity was measured while she was standing and while she was lying down. What difference, if any, in the measurement do you think there would be, and why?
4. If water vapor forms 10% of the gases in air at sea level, what is the partial pressure of water?
5. A patient has pneumonia, and fluids accumulate within the alveoli. Explain why this results in an increased rate of respiration. How can O_2 therapy return this rate to normal?
6. A patient has severe emphysema that has extensively damaged the alveoli and reduced the surface area of the respiratory membrane. Although the patient is receiving O_2 therapy, he still has a tremendous urge to take a breath (i.e., he does not feel as if he is getting enough air). Why does this occur?

7. Patients with diabetes mellitus who are not being treated with insulin therapy rapidly metabolize lipids, and acidic by-products of lipid metabolism accumulate in the bloodstream. How does this affect ventilation? Why is the change in ventilation beneficial?
8. Olivia was hysterical and hyperventilating. The doctor made her breathe into a paper bag. Because you are an especially astute student, you say to the doctor, "When Olivia was hyperventilating, she was reducing blood CO_2 levels; when she breathed into the paper bag, CO_2 was trapped in the bag, and she was rebreathing it, thus causing her blood CO_2 levels to increase. As blood CO_2 levels increased, the urge to breathe should have increased. Instead, she began to breathe more slowly. Please explain." How do you think the doctor would respond? (*Hint:* Recall that the effect of decreased blood CO_2 on the vasomotor center results in vasodilation and a sudden decrease in blood pressure.)
9. Hyperventilating before swimming underwater can increase the time spent under water. Explain. Caution should be taken before hyperventilating before swimming under water. You could pass out while still under water and drown. Explain.
10. The blood pH of a runner was monitored during a race. Shortly after the beginning of the race, her blood pH increased for a short time. Propose an explanation to account for the increased pH values following the start of the race.

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

16

Digestive System

The digestive tract in humans includes the structures for consumption of food, breakdown of food into nutrients, absorption of nutrients, and removal of wastes.

LEARN TO APPLY IT

Demondre complained often of cramps, gas, and diarrhea after eating. Lately, he had been increasingly uncomfortable after lunch at school, where he ate cheese pizza nearly every day. His mother took him to see his doctor, who explained that Demondre should avoid dairy products (which contain the sugar lactose), especially cheese pizza!

Explain why Demondre can no longer eat lactose without side effects.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 16 Digestive System

16.1 FUNCTIONS OF THE DIGESTIVE SYSTEM

Learning Outcome *After reading this section, you should be able to*

A. List the major functions of the digestive system.

Every cell of the body requires nutrients, yet most cells cannot leave their position in the body and travel to a food source. Therefore, the food must be converted to a usable form and then delivered to the cells. The **digestive system** (figure 16.1), with the assistance of the circulatory system, is a complex set of organs, glands, and ducts that work together to transform food into nutrients for cells. Food is taken into the digestive system, where it is broken down into smaller and smaller particles. Enzymes in the digestive system break the particles down into very small molecules, which are absorbed into the blood and transported all over the body. There, those molecules are broken down by other enzymes to release energy or are assembled into new molecules to build tissues and organs. This chapter describes the structure and function of the digestive organs and their accessory glands. Figure 16.2 summarizes the major functions of each portion of the digestive tract.

Figure 16.1 **Digestive System**

The digestive system consists of the digestive tract and associated organs, including the liver and pancreas.

Figure 16.2 APR **Digestive Functions of the Digestive Tract**

Each portion of the digestive tract plays a different role in the breakdown of food and the absorption of nutrients.

The functions of the digestive system include the following:

1. *Ingestion and mastication.* Ingestion is the consumption of solid or liquid food, usually through the mouth. Mastication is chewing.
2. *Propulsion and mixing.* Propulsion is the movement of food from one end of the digestive tract to the other. Mixing is the movement of food back and forth in the digestive tract, which incorporates the digestive system's many secretions into the food.

3. *Digestion and secretion.* Digestion is the breakdown of large organic molecules into smaller molecules that can be absorbed. Digestion occurs through mechanical and chemical means. Secretion is the addition of liquids, enzymes, and mucus to the ingested food.
4. *Absorption.* Absorption is the movement of molecules out of the digestive tract and into the blood or lymphatic system. The epithelial cells that line the lumen of the small intestine absorb the small molecules of nutrients (amino acids, monosaccharides, fatty acids, vitamins, minerals, and water) that result from the digestive process.
5. *Elimination.* Elimination is the removal of undigested material, such as fiber from food, plus other waste products from the body as feces.

16.2 ANATOMY AND HISTOLOGY OF THE DIGESTIVE SYSTEM

Learning Outcome ***After reading this section, you should be able to***

A. Describe the general histology of the digestive tract.

The digestive system consists of the **digestive tract,** or *gastrointestinal* (***GI;*** GAS-troh-in-TESS-tin-al) ***tract,*** plus specific associated organs.

The specific portions of the digestive tract include: (1) the oral cavity (mouth), (2) the pharynx (throat), (3) the esophagus, (4) the stomach, (5) the small and large intestines, and (6) the anus. The specific associated organs of the digestive system are (1) the salivary glands, which empty into the oral cavity, (2) the liver, and (3) the pancreas. Both the liver and pancreas empty into the small intestine.

Because the digestive tract is open at the mouth and anus, the inside of the tract is continuous with the outside environment, and food entering the digestive tract may contain not only useful nutrients but also indigestible components such as fiber, or harmful materials such as bacteria. Therefore, the inner lining of the digestive tract serves as a protective barrier to those indigestible and harmful materials while allowing for the specific absorption of nutrients across the wall of the digestive tract. Once across the wall of the digestive tract, the nutrients enter the blood and are distributed to the tissues of the body.

Various parts of the digestive tract are specialized for different functions. For example, the oral cavity and the esophagus are lined with a stratified epithelium, which protects them from the abrasion of chewing and swallowing. The stomach and intestine are lined with a columnar

epithelium, which is specialized for secretion of digestive fluids and absorption of nutrients. The digestive tract consists of four major tunics, or layers: The four tunics are: (1) the mucosa, (2) the submucosa, (3) the muscularis, and (4) a serosa or an adventitia (figure 16.3):

1. The **mucosa** (myu-KOH-sah) is the innermost tunic and it consists of three layers: (a) the inner **mucous epithelium,** the innermost layer, (b) the **lamina propria,** which is loose connective tissue, and (c) the **muscularis mucosae**, a thin outer layer of smooth muscle.
2. The **submucosa** lies just outside the mucosa. It is a thick layer of loose connective tissue containing nerves, blood vessels, and small glands. An extensive network of nerve cell processes forms a **plexus** (network) within the submucosa. Autonomic nerves innervate this plexus.
3. The **muscularis** lies outside the submucosa. In most parts of the digestive tract it consists of an (a) inner layer of **circular smooth muscle** and (b) an outer layer of **longitudinal smooth muscle.** Another nerve plexus, also innervated by autonomic nerves, lies between the two muscle layers. Together, the nerve plexuses of the submucosa and muscularis compose the **enteric** (en-TER-ik) **nervous system.** This nervous system, which is a division of the autonomic nervous system, is extremely important in controlling movement and secretion within the tract (see chapter 8).
4. The **serosa** is the outermost layer of the digestive tract. It consists of (a) the peritoneum, which is a smooth epithelial layer, and (b) its underlying connective tissue. In regions of the digestive tract not covered by peritoneum, the connective tissue layer is called the **adventitia** (ad-ven-TISH-ah; foreign, coming from outside), rather than serosa. The adventitia is continuous with the surrounding connective tissue.

Figure 16.3 APR **Digestive Tract Histology**

The four tunics are the mucosa, the submucosa, the muscularis, and a serosa or an adventitia. Glands may exist along the digestive tract as part of the epithelium, within the submucosa, or as large glands outside the digestive tract.

Peritoneum

Recall from chapter 1 that the walls of the abdominal cavity and the abdominal organs are associated with a serous membrane (figure 16.4). This membrane is called the peritoneum (per-ih-toh-NEE-um; to stretch over). The serous membrane that covers the organs is the **visceral peritoneum,** or serosa, and is the serous membrane that covers the organs. The **parietal peritoneum** is the serous membrane that lines the wall of the abdominal cavity.

Figure 16.4 APR **Peritoneum and Mesenteries**

The parietal peritoneum lines the abdominal cavity (*blue, dashed line*), and the visceral peritoneum covers abdominal organs (*red lines with small dots*). Retroperitoneal organs are behind the parietal peritoneum. The mesenteries are membranes that connect abdominal organs to each other and to the body wall (*purple lines with larger dots*).

Peritonitis (PER-i-toh-NIGH-tis) is a potentially life-threatening inflammation of the peritoneal membranes. The inflammation can result from chemical irritation by substances, such as bile, that have escaped from the digestive tract. Or it can result from infection originating in the digestive tract, as may occur when an infected appendix ruptures. The main symptoms of peritonitis are acute abdominal pain and tenderness that are worsened by movement.

Many of the organs of the abdominal cavity are held in place by connective tissue sheets called **mesenteries** (MESS-en-ter-rees). The mesenteries also provide a route for blood vessels and nerves from the abdominal wall to the organs. The mesenteries consist of two layers of serous membranes with a thin layer of loose connective tissue between them.

Mesentery is a general term referring to the serous membranes attached to the abdominal organs. Mesentery is also applied specifically to particular mesenteries: (1) the mesentery associated with the small intestine is called the **mesentery proper,** (2) The mesentery connecting the lesser curvature of the stomach to the liver and diaphragm is called the **lesser omentum** (oh-MEN-tum), and (3) The mesentery connecting the greater curvature of the stomach to the transverse colon and posterior body wall is called the **greater omentum.** The greater omentum is unusual in that it is a long, double fold of mesentery that extends inferiorly from the stomach before looping back to the transverse colon to create a cavity, or pocket, called the **omental bursa** (BURR-sah). Adipose tissue accumulates in the greater omentum, giving it the appearance of a fat-filled apron that covers the anterior surface of the abdominal viscera.

Understand

Apply It 1

If you placed a pin completely through both folds of the greater omentum, through how many layers of simple squamous epithelium would the pin pass?

Other abdominal organs that have no mesenteries are referred to as **retroperitoneal** (RE-troh-PER-i-toh-NEE-uhl; behind the peritoneum; see chapter 1). The retroperitoneal organs lie along the abdominal wall and include the duodenum, pancreas, ascending colon, descending colon, rectum, kidneys, adrenal glands, and urinary bladder.

16.3 ORAL CAVITY, PHARYNX, AND ESOPHAGUS

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the structure of a tooth.
B. Describe the major salivary glands.
C. Compare the structures and functions of the salivary glands.
D. Describe mastication and swallowing.

Anatomy of the Oral Cavity

The **oral cavity** (figure 16.5), or mouth, is divided into two regions: (1) the space between the lips or cheeks and the teeth, and (2) the oral cavity proper, which lies inside the teeth and houses the tongue.

Figure 16.5 APR **Oral Cavity**
The oral cavity is the normal location for ingestion of liquid and solid food.

Lips, Cheeks, and Tongue

Lips

The **lips** are muscular structures, formed mostly by the **orbicularis oris** (or-BIK-you-LAH-ris OR-is) **muscle** (see figure 7.16). The outer surfaces of the lips are covered by skin. The keratinized stratified epithelium of the skin becomes thin at the margin of the lips. The color from the underlying blood vessels can be seen through the thin, transparent epithelium, giving the lips a reddish-pink appearance. At the internal margin of the lips, the epithelium is continuous with the moist stratified squamous epithelium of the mucosa in the oral cavity.

Cheeks

The cheeks form the lateral walls of the oral cavity. Located within the cheeks are the **buccinator** (BUK-si-NAY-tor) **muscles** (see figure 7.16 and chapter 7), which flatten the cheeks against the teeth. The lips and cheeks are important in the process of **mastication** (mas-tih-KAY-shun), or chewing. Mastication begins the process of mechanical digestion, which breaks down large food particles into smaller ones. The lips and cheeks move the food around within the oral cavity and hold the food in place while the teeth crush or tear it. The cheeks also help form words during the speech process.

Tongue

The **tongue** is a large, muscular organ that occupies most of the oral cavity. The major attachment of the tongue is in the posterior part of the oral cavity. The anterior part of the tongue is relatively free, except for an anterior attachment to the floor of the mouth by a thin fold of tissue called the **frenulum** (FREN-you-lum) (figure 16.5). The muscles associated with the tongue are described in chapter 7. The anterior two-thirds of the tongue is covered by papillae, some of which contain taste buds (see chapter 9). The posterior one-third of the tongue is devoid of papillae and has only a few scattered taste buds. In addition, the posterior portion contains a large amount of lymphatic tissue, which helps form the lingual tonsil (see chapter 14).

The tongue moves food in the mouth and, in cooperation with the lips and cheeks, holds the food in place during mastication. It also plays a major role in the process of swallowing. In addition, the tongue is a major sensory organ for taste, as well as one of the major organs of speech.

Teeth

There are 32 **teeth** in the normal adult mouth, located in the mandible and maxillae. The teeth can be divided into quadrants: (1) right upper, (2) left upper, (3) right lower, and (4) left lower.

In adults, each quadrant contains (1) one central, (2) one lateral **incisor** (in-SIGH-zor; to cut), (3) one **canine** (KAH-nine; dog), (4) first and second **premolars** (pree-MOH-lars; *molaris,* a millstone), and (5) first, second, and third **molars** (MOH-lars). The third molars are called **wisdom teeth** because they usually appear in the late teens or early twenties, when the person is old enough to have acquired some degree of wisdom.

The teeth of adults are called **permanent teeth,** or *secondary teeth* (figure 16.6*a*). Most of them are replacements for the 20 **primary teeth,** or *deciduous* (de-si-DEW-us) *teeth,* also called milk or baby teeth, which are lost during childhood (figure 16.6*b*).

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Figure 16.6 **Teeth**

(*a*) Permanent teeth. (*b*) Deciduous teeth. Dental professionals have developed a "universal" numbering and lettering system for convenience in identifying individual teeth.

Each tooth consists of three regions: (1) a **crown** with one or more **cusps** (points), (2) a **neck,** and (3) a **root** (figure 16.7). The crown is the visible portion of a tooth. The neck is the small region between the crown and the root. The root is the largest region of the tooth and anchors it in the bone of the maxillae and mandible.

Figure 16.7 **Molar Tooth in Place in the Alveolar Bone**

A tooth consists of a crown, a neck, and a root. The root is covered with cementum, and the tooth is held in the socket by periodontal ligaments. Nerves and vessels enter and exit the tooth through a foramen in the part of the root deepest in the alveolus.

The bulk of the tooth is formed by a living, cellular, calcified tissue called dentin (DEN-tin; dens, tooth). In the crown region of the tooth, the dentin is covered by an extremely hard, acellular substance called enamel, which protects the tooth against abrasion and acids produced by bacteria in the mouth. The surface of the dentin in the root is covered with cementum (se-men′tŭm), which helps anchor the tooth in the jaw. Within the center of the tooth is a hollow space called the **pulp cavity.** The pulp cavity is filled with a material called **pulp,** which consists of blood vessels, nerves, and connective tissue, called **pulp.** The pulp cavity is surrounded by dentin.

The teeth are held in place within pockets in the bone, called **alveoli** (al-VEE-oh-lie; sockets). The alveoli are found along the alveolar processes of the mandible and maxillae. The alveolar processes are covered by dense fibrous connective tissue and moist stratified squamous epithelium, referred to as the **gingiva** (JIN-jih-vah), or gums. **Periodontal** (PER-ee-oh-DON-tal; around the teeth) **ligaments** secure the teeth in the alveoli by embedding into the cementum.

Formation of **dental caries** (kār′ēz), or tooth decay, is the result of the breakdown of enamel by acids produced by bacteria on the tooth surface. Enamel is nonliving and cannot repair itself. Consequently, a dental filling is necessary to prevent further damage. **Periodontal disease** is

inflammation and degeneration of the periodontal ligaments, gingiva, and alveolar bone. This disease is the most common cause of tooth loss in adults. An infection may occur in a tooth, in the bone, or in the surrounding soft tissues. The infection may cause enlargement of the superior cervical lymph nodes. This is because all lymphatic drainage from the face goes through these nodes.

Palate and Tonsils

The **palate** (PAL-uht), or roof of the oral cavity, separates the oral cavity from the nasal cavity and prevents food from passing into the nasal cavity during chewing and swallowing. The palate consists of two parts: (1) the hard palate and (2) the soft palate. The **hard palate** is the anterior part and contains bone. The **soft palate** is the posterior part and consists of skeletal muscle and connective tissue (see figure 16.5). The **uvula** (YOU-vyu-lah; a grape) is a posterior extension of the soft palate.

The **tonsils** (TON-sills) are located in the lateral posterior walls of the oral cavity, in the nasopharynx, and in the posterior surface of the tongue. The tonsils are described in chapter 14.

Salivary Glands

There are three major pairs of **salivary** (SAL-ih-var-ee) **glands:** (1) the parotid glands, (2) the submandibular glands, and (3) the sublingual glands (figure 16.8). A considerable number of other salivary glands are scattered throughout the oral cavity, including on the tongue. Salivary glands produce **saliva** (sa-LIE-vah). Saliva is a mixture of **serous** (watery) and **mucous** fluids and has multiple roles. The salivary glands are compound alveolar glands. They have branching ducts with clusters of alveoli, resembling grapes, at the ends of the ducts (see chapter 4).

Figure 16.8 APR **Salivary Glands**

The large salivary glands are the parotid glands, the submandibular glands, and the sublingual glands.

The largest of the salivary glands, the **parotid** (pah-ROT-id; beside the ear) **glands,** are serous glands located just anterior to each ear. Parotid ducts enter the oral cavity adjacent to the second upper molars.

Mumps is an inflammation of the parotid gland caused by a viral infection. The inflamed parotid glands become swollen, often making the cheeks quite large. The virus causing mumps can also infect other structures. Mumps in an adult male may involve the testes and can result in sterility.

The **submandibular** (sub-man-DIB-you-lar; below the mandible) **glands** produce more serous than mucous secretions. Each gland can be felt as a soft lump along the inferior border of the mandible. The submandibular ducts open into the oral cavity on each side of the frenulum of the tongue (see figure 16.5).

The **sublingual** (sub-LING-wal; below the tongue) **glands,** the smallest of the three paired salivary glands, produce primarily mucous secretions. They lie immediately below the mucous membrane in the floor of the oral cavity. Each sublingual gland has 10–12 small ducts opening onto the floor of the oral cavity.

Saliva

Saliva is composed of fluid and proteins and has three main functions (table 16.1): (1) it helps keep the oral cavity moist, which is needed for

normal speech and for dissolving food particles so they can be tasted, (2) it has protective functions, and (3) it begins the process of digestion.

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TABLE 16.1 Functions of Major Digestive System Secretions

Organ or Region	Creation	Function
Oral Cavity	Serous saliva (mostly water, bicarbonate ions) Salivary glands Mucus Lysozyme	Moistens food and mucous membrane; neutralizes bacterial acids; flushes bacteria from oral cavity Digests carbohydrates Lubricates food; protects digestive tract from digestion Has mild antibacterial activity
Stomach	Hydrochloric acid Pepsin* Mucus Intrinsic factor Gastric lipase	Antibacterial; decreases stomach pH to activate pepsinogen to pepsin Digests protein into smaller peptide chains; activates pepsinogen Protects stomach lining from acid and digestion Binds to vitamin B_{12} and aids in its absorption in the small intestine
Liver	Bile	Bile salts in bile emulsify lipids, making them available to lipases, and help make end products soluble and available for absorption by the intestinal mucosa; many of the other bile contents are waste products, such as bile pigments, that are transported to the intestines for disposal

Organ or Region	Creation	Function
Pancreas	Trypsin*	Digests proteins (cleaves at arginine or lysine amino acids); activates trypsinogen and other digestive enzymes
	Chymotrypsin*	Digests proteins (cleaves at hydrophobic amino acids)
	Carboxypeptidase*	Digests proteins (removes amino acids from the carboxyl end of proteins)
	Pancreatic amylase	Digests carbohydrates (hydrolyzes starches and glycogen to form maltose and isomaltose)
	Pancreatic lipase	Digests lipids (breaks down triglycerides into monoglycerides and free fatty acids)
	Cholesterol esterase	Digests cholesteryl esters (breaks down into cholesterol and free fatty acid)
	Ribonuclease	Digests ribonucleic acid (hydrolyzes phosphodiester bonds)
	Deoxyribonuclease	Digests deoxyribonucleic acid (hydrolyzes phosphodiester bonds)
	Bicarbonate ions	Neutralize acid from stomach; provide appropriate pH for pancreatic enzymes
Small Intestine	Mucus	Protects duodenum from stomach acid, and intestinal wall from digestive enzymes
	Peptidases†	Split amino acids from polypeptides
	Enterokinase†	Activates trypsin from trypsinogen
	Sucrase†	Splits sucrose into glucose and fructose
	Maltase†	Splits maltose into two glucose molecules
	Isomaltase†	Splits isomaltose into two glucose molecules
	Lactase†	Splits lactose into glucose and galactose

Organ or Region	Creation	Function
Large Intestine	Mucus	Provides adhesion for fecal matter; protects intestinal wall from bacterial acids and actions

*These enzymes are secreted as inactive forms, then activated.

**These enzymes remain in the microvilli.

The normal daily rate of saliva secretion varies from approximately 0.5 L to 1.5 L. The serous part of saliva, produced mainly by the parotid and submandibular glands, contains a digestive enzyme called **salivary amylase** (AM-il-ace) (table 16.1), which breaks down starch. Salivary amylase breaks the covalent bonds between glucose molecules in starch and other polysaccharides. This produces disaccharides such as maltose and isomaltose. Maltose and isomaltose have a sweet taste; thus, the digestion of polysaccharides by salivary amylase enhances the sweet taste of food.

CLINICAL IMPACT

Dietary Fiber

Even though humans cannot digest cellulose, it is important to normal digestive function. Cellulose provides bulk, or fiber, in the diet. The presence of this bulk facilitates movement of material through the digestive tract by providing mass against which the muscular wall of the digestive tract can push. In the 1950s, some nutritionists speculated that eventually all the nutrients we need could be reduced into a single tablet and that we no longer would have to eat food. It is now known that indigestible bulk is very important to the normal function of the digestive tract. Adults should consume fiber in the form of cellulose, such as is found in bran and legumes, pectin from certain fruits such as apples and pears, and beta-glucan from oats and barley, among others. Dietary fiber is classified as either soluble or insoluble fiber. Soluble fiber binds fat and cholesterol in the intestines, lowering low-density lipoprotein concentrations in the blood, and slows the absorption of glucose,

preventing a glucose surge and insulin spike. Insoluble fiber helps to push food through the intestinal tract, preventing constipation, and dilutes carcinogens.

However, food spends very little time in the mouth. Consequently, only about 5% of the total carbohydrates humans absorb are digested in the mouth. Also, most starches are contained in plant cells, which are surrounded by cell walls composed primarily of the polysaccharide **cellulose** (SEL-you-lohs). Humans lack the necessary enzymes to digest cellulose. Cooking and thorough chewing of food disrupt the cellulose covering and increase the efficiency of the digestive process.

Saliva has several protective functions.

1. It prevents bacterial infections in the mouth by washing the oral cavity with a mildly antibacterial enzyme, called **lysozyme** (LIE-soh-zime).
2. Saliva also neutralizes the pH in the mouth, which reduces the harmful effects of bacterial acids on tooth enamel.
3. The neutralization effect of saliva prevents the ulceration and infection of the oral mucosa and caries (cavities) formation in the teeth.

The serous part of saliva dissolves molecules, which must be in solution to stimulate taste receptors. The mucous secretions of the submandibular and sublingual glands contain a large amount of **mucin** (MYU-sin), a proteoglycan that gives a lubricating quality to the secretions of the salivary glands.

Salivary gland secretion is regulated primarily by the autonomic nervous system, with parasympathetic stimulation being the most important. Salivary secretions increase in response to a variety of stimuli, such as tactile stimulation in the oral cavity and certain tastes, especially sour. Higher brain centers can stimulate parasympathetic activity and thus increase the activity of the salivary glands in response to the thought of food, to odors, or to the sensation of hunger. Sympathetic stimulation increases the mucous content of saliva. When a person becomes frightened and the sympathetic division of the autonomic nervous system is stimulated, the person may have a dry mouth with thick mucus.

Mastication

Food taken into the mouth is chewed, or masticated, by the teeth. The incisors and canines primarily cut and tear food, whereas the premolars and molars primarily crush and grind it. Mastication breaks large food particles into many small ones, which have a much larger total surface area

than a few large particles would have. Because digestive enzymes act on molecules only at the surface of the food particles, mastication increases the efficiency of digestion.

Pharynx

The **pharynx** (FAIR-inks), or throat, which connects the mouth with the esophagus, consists of three parts: (1) the nasopharynx, (2) the oropharynx, and (3) the laryngopharynx (see chapter 15). Normally, only the oropharynx and laryngopharynx carry food to the esophagus. The posterior walls of the oropharynx and laryngopharynx are formed by the superior, middle, and inferior **pharyngeal constrictor muscles.**

Esophagus

The **esophagus** (ee-SOF-ah-gus; gullet) is a muscular tube, lined with moist stratified squamous epithelium, that extends from the pharynx to the stomach. It is about 25 centimeters (cm) long and lies anterior to the vertebrae and posterior to the trachea within the mediastinum. The upper one-third of the esophagus has skeletal muscle in its wall, the middle third has a mixture of both skeletal and smooth muscle fibers, while the lower one-third has smooth muscle in its wall. It passes through the diaphragm and ends at the stomach. The esophagus plays an important role in swallowing, which transports food from the pharynx to the stomach. To aid in movement of food to the stomach, upper and lower **esophageal sphincters,** located at the upper and lower ends of the esophagus, respectively, regulate the movement of food into and out of the esophagus (see "Swallowing"). The lower esophageal sphincter is sometimes called the **cardiac sphincter.** Numerous mucous glands produce a thick, lubricating mucus that coats the inner surface of the esophagus.

Swallowing

Swallowing, or *deglutition* (dee-glue-TISH-un), can be divided into three phases: (1) the voluntary phase, (2) the pharyngeal phase, and (3) the esophageal phase. Figure 16.9 outlines the events during the three phases of swallowing.

PROCESS Figure

PROCESS Figure 16.9 APR **Events During the Three Phases of Swallowing**

The three phases of swallowing are: voluntary, pharyngeal, and esophageal.

Understand **Explain why it may be difficult to swallow if you have a sore throat.**

❶ During the **voluntary phase,** a bolus, or mass of food, is formed in the mouth. The tongue pushes the bolus against the hard palate. This forces the bolus toward the posterior part of the mouth and into the oropharynx.

❷ The **pharyngeal phase** of swallowing is controlled by a reflex. This phase is initiated when a bolus of food stimulates receptors in the oropharynx to elevate the soft palate, closing off the nasopharynx. The pharynx elevates to receive the bolus of food from the mouth. The three **pharyngeal constrictor muscles** then contract in succession, forcing the food through the pharynx. At the same time, the upper esophageal sphincter relaxes, and food is pushed into the esophagus. As food passes through the pharynx, the vestibular and vocal folds close, and the **epiglottis** (ep-ih-GLOT-is; upon the glottis, opening of the larynx) is tipped posteriorly, so that the opening into the larynx is covered. These movements prevent food from passing into the larynx.

❸ The **esophageal phase** of swallowing is responsible for moving food from the pharynx to the stomach. Muscular contractions of the esophagus occur in **peristaltic** (per-ih-STAL-tik; *peri,* around + *stalsis,* constriction) **waves.**

Understand

Apply It 2

What would happen if a person had a cleft of the soft palate, so that the soft palate did not completely close the passage between the nasopharynx and the oropharynx during swallowing? What happens if a person has an explosive burst of laughter while trying to swallow a liquid? What happens if a person tries to swallow and speak at the same time?

Figure 16.10 illustrates the process of peristalsis.

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PROCESS Figure

PROCESS Figure 16.10 **Peristalsis**

Waves of smooth muscle contraction push digesting food and waste through the digestive tract.

Some causes of diarrhea increase peristalsis of the intestine. Explain how medications that slow intestinal motility relieve symptoms of diarrhea (see Systems Pathology, "Diarrhea").

❶ The upper esophageal sphincter relaxes, allowing the bolus of food to enter the esophagus. A wave of relaxation of the esophageal muscles precedes the bolus of food down the esophagus.

❷ A wave of strong contraction of the circular muscles follows and propels the bolus through the esophagus. Gravity assists the movement of material, especially liquids, through the esophagus. However, the peristaltic contractions that move material through the esophagus are sufficiently forceful to allow a person to swallow even while doing a headstand or floating in the zero-gravity environment of space. The peristaltic contractions cause relaxation of the lower esophageal

sphincter in the esophagus as the peristaltic waves approach the stomach and food is permitted to enter the stomach.

16.4 STOMACH

Learning Outcomes ***After reading this section, you should be able to***

A. Outline the anatomical and physiological characteristics of the stomach.
B. Describe the stomach secretions, their functions, and their regulation.
C. Describe gastric movements and stomach emptying.
D. Describe how gastric movements and stomach emptying are regulated.

Anatomy of the Stomach

The stomach is divided into four regions: (1) cardiac part, (2) fundus, (3) body, and (4) pyloric part (figure 16.11). The esophagus opens into the **cardiac part** of the stomach at the **gastro-esophageal** opening. The part of the stomach to the left of the cardiac part, the **fundus** (FUN-dus), is actually superior to the cardiac opening. The largest part of the stomach is the **body,** which turns to the right, creating a *greater curvature* and a *lesser curvature*. The body narrows to form the funnel-shaped **pyloric** (pie-LOR-ik; gatekeeper) **part** of the stomach. The pyloric part opens into the small intestine and is surrounded by the **pyloric sphincter,** a relatively thick ring of smooth muscle. The pyloric sphincter helps regulate the movement of gastric contents into the small intestine.

Figure 16.11 **Anatomy and Histology of the Stomach**

(*a*) Cutaway section reveals muscular layers and internal anatomy. (*b*) A section of the stomach wall illustrates its histology, including several gastric pits and glands. (*c*) Photomicrograph of gastric glands.

(c) ©Victor Eroschenko

The muscularis layer of the stomach is different from other regions of the digestive tract in that it consists of three layers: (1) an outer longitudinal layer, (2) a middle circular layer, and (3) an inner oblique

layer. These muscular layers produce a churning action in the stomach, important in the digestive process. The submucosa and mucosa of the stomach are arranged in large folds called **rugae** (ROO-gee; wrinkles) when the stomach is empty (figure 16.11*a*). These folds allow the mucosa and submucosa to stretch, and the folds disappear as the stomach is filled.

The stomach is lined with simple columnar epithelium. The mucosal surface forms numerous tubelike **gastric pits** (figure 16.11*b*), which are the openings for the **gastric glands.** The epithelial cells of the stomach can be divided into five groups: (1) surface mucous cells, (2) mucous neck cells, (3) parietal cells, (4) endocrine cells, and (5) chief cells. All but the surface mucous cells are found within the gastric glands. The functions of each of the groups is as follows:

1. **Surface mucous cells**, which are found on the inner surface of the stomach and lining the gastric pits. These cells produce mucus that coats and protects the stomach lining.
2. **mucous neck cells,** which produce mucus;
3. **parietal cells,** which produce hydrochloric acid and intrinsic factor;
4. **endocrine cells,** which produce regulatory hormones and paracrine signal molecules; and
5. **chief cells,** which produce **pepsinogen** (pep-SIN-oh-jen), a precursor of the protein-digesting enzyme **pepsin** (PEP-sin; *pepsis,* digestion).

Secretions of the Stomach

As food enters the stomach, the food is mixed with stomach secretions to become a semifluid mixture called **chyme** (KIME; juice). Although some digestion occurs in the stomach, that is not its principal function.

Stomach secretions from the gastric glands include four substances (table 16.1):

1. **Hydrochloric acid** produces a pH of about 2.0 in the stomach. The acid kills microorganisms and activates the enzyme, pepsin.
2. **Pepsin** is converted from its inactive form, called pepsinogen. Pepsin breaks covalent bonds of proteins to form smaller peptide chains. Pepsin exhibits optimum enzymatic activity at a pH of about 2.0.
3. **Mucus** forms a thick layer, which lubricates the epithelial cells of the stomach wall and protects them from the damaging effect of the acidic

chyme and pepsin. Irritation of the stomach mucosa stimulates the secretion of a greater volume of mucus.

4. **Intrinsic** (in-TRIN-sik) **factor** binds with vitamin B_{12} and makes it more readily absorbed in the small intestine. Vitamin B_{12} is important in deoxyribonucleic acid (DNA) synthesis and in red blood cell production.

Heartburn, or *gastritis,* is a painful or burning sensation in the chest usually associated with an increase in gastric acid secretion and/or a backflush of acidic chyme into the esophagus. Overeating, eating fatty foods, lying down immediately after a meal, consuming too much alcohol or caffeine, smoking, and wearing extremely tight clothing can all cause heartburn. Medications can relieve the symptoms of heartburn by blocking gastric acid secretion. Some medications block histamine stimulation of acid release from parietal cells, while other medications block the proton pump in parietal cells that generates gastric acid. Antacids neutralize acids already secreted into the stomach.

Regulation of Stomach Secretions

Approximately 2 L of gastric secretions (gastric juice) are produced each day. Both nervous and hormonal mechanisms regulate gastric secretions. The neural mechanisms involve central nervous system (CNS) reflexes integrated within the medulla oblongata. Higher brain centers can influence these reflexes. Local reflexes are integrated within the enteric plexus in the wall of the digestive tract and do not involve the CNS. Hormones produced by the stomach and intestine help regulate stomach secretions.

Regulation of stomach secretions can be divided into three phases: (1) the cephalic phase, (2) the gastric phase, and (3) the intestinal phase. The cephalic phase can be viewed as the “get started” phase, when the stomach secretions are increased in anticipation of incoming food. This is followed by the gastric, “go for it,” phase, when most of the stimulation of secretion occurs. Finally, the intestinal phase is the “slow down” phase, during which stomach secretion decreases. Figure 16.12 outlines the steps that regulate each phase of stomach secretion.

PROCESS Figure

negative-

PROCESS Figure 16.12 APR **Regulation of Stomach Secretions**

There are three phases of stomach secretions: cephalic, gastric, and intestinal.

Why is it advantageous to the overall digestive process for secretin and cholecystokinin to slow stomach emptying upon initiation of the intestinal phase?

Cephalic Stage (Get Started!)

The cephalic phase is the brain phase of stomach secretion. It is controlled by the CNS. It begins even before the bolus of food enters the stomach.

1. The taste, smell, or thought of food or tactile sensations of food in the mouth stimulate the medulla oblongata.
2. Action potentials are sent from the medulla oblongata along parasympathetic axons within the vagus nerves to the stomach. Within the stomach wall, the preganglionic neurons stimulate postganglionic neurons in the enteric plexus.
3. The postganglionic neurons stimulate secretory activity in the cells of the stomach mucosa, causing the release of hydrochloric acid, pepsin, mucus, and intrinsic factor. The neurons also stimulate the release of gastrin and histamine from endocrine cells.
4. **Gastrin** (GAS-trin) is a hormone that enters the blood and is carried back to the stomach, where it stimulates additional secretory activity (table 16.2). Histamine is both a paracrine chemical signal that acts locally and a hormone that enters the blood to stimulate gastric gland secretory activity. Histamine is the most potent stimulator of hydrochloric acid secretion. Drugs that block the actions of histamine can lower acid levels.

Table 16.2 Functions of the Major Digestive System Hormones

Hormone	Source	Function
Gastrin	Gastric glands	Increases gastric secretions
Secretin	Duodenum	Decreases gastric secretions Increases pancreatic and bile secretions high in bicarbonate ions Decreases gastric motility

Hormone	Source	Function
Cholecystokinin	Duodenum	Decreases gastric secretions Strongly decreases gastric motility Increases gallbladder contraction Increases pancreatic enzyme secretion

Gastric Phase (Go for It!)

The gastric phase of stomach secretion produces the greatest volume of gastric secretions.

❶ The gastric phase is activated by the presence of food in the stomach.

❷ Distention of the stomach stimulates mechanoreceptors (stretch receptors) and activates a parasympathetic reflex. Action potentials generated by the mechanoreceptors are carried by the vagus nerves to the medulla oblongata.

❸ Distention of the stomach also activates local reflexes that increase stomach secretions.

❹ Peptides, produced by the action of pepsin on proteins, stimulate the secretion of gastrin. Gastrin is carried through the blood back to the stomach, where, along with histamine, it stimulates secretion.

Intestinal Phase (Slow Down!)

The intestinal phase of gastric secretion inhibits gastric secretions.

❶ The **intestinal phase** is controlled by the entrance of acidic chyme into the duodenum, which initiates both neural and hormonal mechanisms. When the pH of the chyme entering the duodenum drops to 2.0 or below, the inhibitory influence of the intestinal phase is greatest.

❷ Acidic chyme (pH < 2.0) in the duodenum inhibits CNS stimulation and initiates local reflexes that inhibit gastric secretion. Chemoreceptors in the duodenum are stimulated by H^+ (low pH) or lipids. Action potentials generated by the chemoreceptors are carried by the vagus nerves to the medulla oblongata, where they inhibit parasympathetic action potentials, thereby decreasing gastric secretions.

❸ Local reflexes activated by H^+ or lipids also inhibit gastric secretion.

❹ The hormone **secretin** (se-KREE-tin), which inhibits gastric secretions, is released from the duodenum in response to low pH (table 16.2). Fatty acids and peptides in the duodenum initiate the release of the

hormone **cholecystokinin** (KOH-leh-sis-toh-KIE-nin), which also inhibits gastric secretions (table 16.2).

To summarize, gastric acid secretion is controlled by negative-feedback loops involving nerves and hormones. During the gastric phase, high acid levels in the stomach trigger a decrease in additional acid secretion. Then during the intestinal phase, acidic chyme entering the duodenum triggers a decrease in gastric acid secretion. These negative-feedback loops ensure that the acidic chyme entering the duodenum is neutralized, which is required for the digestion of food by pancreatic enzymes and for the prevention of peptic ulcer formation.

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Movement in the Stomach

Two types of stomach movement aid digestion and help move chyme through the digestive tract: (1) mixing waves and (2) peristaltic waves. Both types of movement result from smooth muscle contractions in the stomach wall. The contractions occur about every 20 seconds and proceed from the body of the stomach toward the pyloric sphincter. Figure 16.13 illustrates the types of movement in the stomach.

❶ Relatively weak contractions result in **mixing waves,** which thoroughly mix ingested food with stomach secretions to form chyme.

❷ In the mixing wave, the more fluid part of the chyme is pushed toward the pyloric sphincter, whereas the more solid center moves back toward the body of the stomach.

❸ Stronger contractions result in **peristaltic waves,** which force the chyme toward and through the pyloric sphincter. The pyloric sphincter usually remains closed because of mild tonic contraction.

❹ Again, the more fluid part of the chyme is pushed toward the pyloric region, whereas the more solid center of the chyme squeezes past the peristaltic constriction back toward the body of the stomach.

❺ Each peristaltic contraction is sufficiently strong to cause partial relaxation of the pyloric sphincter and to pump a few milliliters of chyme through the pyloric opening and into the duodenum. Increased motility leads to increased emptying.

PROCESS Figure

PROCESS Figure 16.13 **Movements in the Stomach**

Food is mixed with hydrochloric acid and other secretions in the stomach to create chyme.

In a person suffering from heartburn, the gastroesophageal opening is weakened and stomach acid can be forced from the stomach back into the esophagus. Explain why medications that slow stomach movements and emptying may worsen heartburn symptoms.

Peristaltic waves also occur when the stomach is empty. These peristaltic waves are increased by low blood glucose levels and can create uncomfortable sensations called **hunger pangs.** Hunger pangs occur for about 2–3 minutes and can build in strength to a prolonged, or tetanic, contraction. Hunger pangs usually begin 12 to 24 hours after the previous meal; in less time for some people. If nothing is ingested, hunger pangs reach their maximum intensity within 3 or 4 days and then become progressively weaker. Sometimes having hunger pangs is referred to as the stomach "growling."

If the stomach empties too fast, the efficiency of digestion and absorption in the small intestine is reduced. However, if the rate of emptying is too slow, the highly acidic contents of the stomach may damage the stomach wall. To prevent these two extremes, stomach emptying is regulated. The hormonal and neural mechanisms that stimulate stomach secretions also increase stomach motility, so that the increased secretions are effectively mixed with the stomach contents. The major stimulus of gastric motility and emptying is distension of the stomach wall. Inhibition of gastric motility and emptying is accomplished by the same negative-feedback loops associated with the intestinal phase of gastric secretion. In particular, cholecystokinin is a major inhibitor of motility and emptying (table 16.2). Hence, stomach emptying is slower after a fatty meal due to the release of cholecystokinin.

Vomiting is usually a protective mechanism against the ingestion of toxic or harmful substances. Vomiting and associated nausea (feeling likely to vomit) can result from irritation anywhere along the digestive tract. Neural stimuli travel along the vagus nerve to the vomiting center in the medulla oblongata. Many antinausea medications work by inhibiting the actions of various neurotransmitters in the vomiting center.

16.5 SMALL INTESTINE

Learning Outcomes *After reading this section, you should be able to*

A. List the characteristics of the small intestine that account for its large surface area.

B. Describe the secretions and movements that occur in the small intestine.

Anatomy of the Small Intestine

The major function of the small intestine is the absorption of nutrients. Most absorption occurs in the first and second portions of the small intestine, although some absorption also occurs in the third portion of the small intestine (see section 16.8, "Digestion, Absorption, and Transport"). The **small intestine** is about 6 meters (m) long and consists of three parts: (1) the duodenum, (2) the jejunum, and (3) the ileum (figure 16.14). The **duodenum** (du-oh-DEE-num) is about 25 cm long (the term *duodenum* means 12, suggesting that it is 12 in. long). The **jejunum** (je-JEW-num) is about 2.5 m long and makes up two-fifths of the total length of the small intestine. The **ileum** (ILL-ee-um) is about 3.5 m long and makes up three-fifths of the small intestine.

Figure 16.14 **Small Intestine**
The small intestine consists of three segments: the duodenum, the jejunum, and the ileum.

The duodenum nearly completes a 180-degree arc as it curves within the abdominal cavity. Part of the pancreas lies within this arc. The **common**

bile duct from the liver and the **pancreatic duct** from the pancreas join and empty into the duodenum (see figure 16.18).

CLINICAL IMPACT

Peptic Ulcers

Approximately 10% of people in the United States will develop a peptic ulcer during their lifetime. Peptic ulcers are caused when the gastric juices (acid and pepsin) digest the mucosal lining of the digestive tract. Peptic ulcers can occur in the duodenum, stomach, or esophagus.

Nearly all peptic ulcers are due to infection by a specific bacterium, *Helicobacter pylori*, which is also linked to gastritis and gastric cancer. Because diet, stress, smoking, and alcohol cause excess acid secretion in the stomach, these lifestyle patterns were deemed responsible for ulcers for many years. Although these factors can contribute to ulcers, it is now clear that the root cause is *H. pylori*.

Antibiotic treatment to eradicate *H. pylori* is the best therapy for ulcers. Other treatments involve drugs that prevent histamine-stimulated acid secretion or that directly inhibit the proton pumps that secrete the acid, but these are only temporary.

The small intestine is the major site of digestion and absorption of food, which are accomplished due to the presence of a large surface area. The small intestine has three modifications that increase its surface area about 600-fold:

1. *Circular folds.* The mucosa and submucosa form a series of **circular folds** that run perpendicular to the long axis of the digestive tract (figure 16.15*a*).
2. *Villi.* Tiny, fingerlike projections of the mucosa form numerous **villi** (VILL-eye; sing. villus), which are 0.5–1.5 mm long (figure 16.15*b*). Each villus is covered by simple columnar epithelium. Within the loose connective tissue core of each villus are a blood capillary network and a lymphatic capillary called a **lacteal** (LAK-tee-al; resembling milk) (figure 16.14). The blood capillary network and the lacteal are very important in transporting absorbed nutrients.
3. *Microvilli.* Most of the cells composing the surface of the villi have numerous cytoplasmic extensions, called **microvilli** (my-kroh-VIL-eye)

(figure 16.15*c*,*d*).

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Figure 16.15 APR **Anatomy and Histology of the Duodenum**

(*a*) Wall of the duodenum, showing the circular folds. (*b*) Villi on a circular fold. (*c*) A single villus, showing the lacteal and capillary network. (*d*) Transmission electron micrograph of microvilli on the surface of a villus.

(d) ©Steve Gschmeissner/Science Source RF

The mucosa of the small intestine is simple columnar epithelium with four major cell types:

1. **absorptive cells,** which have microvilli, produce digestive enzymes, and absorb digested food;
2. **goblet cells,** which produce a protective mucus;

3. **granular cells,** which may help protect the intestinal epithelium from bacteria; and
4. **endocrine cells,** which produce regulatory hormones.

The epithelial cells are located within tubular glands of the mucosa, called **intestinal glands** or *crypts of Lieberkühn,* at the base of the villi. Granular and endocrine cells are located in the bottom of the glands. The submucosa of the duodenum contains mucous glands, called **duodenal glands,** which open into the base of the intestinal glands.

The duodenum, jejunum, and ileum are similar in structure. However, progressing from the duodenum through the ileum, there are gradual decreases in the diameter of the small intestine, in the thickness of the intestinal wall, in the number of circular folds, and in the number of villi. Lymphatic nodules are common along the entire length of the digestive tract, and clusters of lymphatic nodules, called **Peyer patches,** are numerous in the ileum. These lymphatic tissues help protect the intestinal tract from harmful pathogens.

The site where the ileum connects to the large intestine is called the **ileocecal** (ILL-ee-oh-SEE-cal) **junction.** It has a ring of smooth muscle, the **ileocecal sphincter ,** and an **ileocecal valve** (see figure 16.22*a*), which allow the intestinal contents to move from the ileum to the large intestine, but not in the opposite direction.

Secretions of the Small Intestine

Secretions from the mucosa of the small intestine contain mainly mucus, ions, and water. Intestinal secretions lubricate and protect the intestinal wall from the acidic chyme and the action of digestive enzymes. They also keep the chyme in the small intestine in a liquid form to facilitate the digestive process. Most of the secretions entering the small intestine are produced by the intestinal mucosa, but the secretions of the liver and the pancreas also enter the small intestine and play important roles in digestion.

The epithelial cells in the walls of the small intestine have two major enzyme groups, bound to their free surfaces, These enzyme groups include: (1) peptidases and (2) disaccharidases. **Peptidases** (PEP-ti-days) digest proteins. They break the peptide bonds in proteins to form amino acids. **Disaccharidases** (dye-SAK-ah-rid-ase-ez) digest small sugars, specifically disaccharides. The disaccharidases break down disaccharides, such as

maltose, into monosaccharides, such as glucose. The intestinal epithelium absorbs the resulting amino acids and monosaccharides (see table 16.1).

Mucus is produced by duodenal glands and by goblet cells, which are dispersed throughout the epithelial lining of the entire small intestine and within intestinal glands. Hormones released from the intestinal mucosa stimulate liver and pancreatic secretions. The vagus nerve, secretin release, and chemical or tactile irritation of the duodenal mucosa all stimulate secretion by duodenal glands.

Movement in the Small Intestine

Mixing and propulsion of chyme are the primary mechanical events that occur in the small intestine. **Peristaltic contractions** proceed along the length of the intestine for variable distances and cause the chyme to move along the small intestine (see figure 16.10). **Segmental contractions** are propagated for only short distances and mix intestinal contents. Figure 16.16 illustrates how segmental contractions aid in mixing intestinal contents.

❶ A secretion introduced into the digestive tract or into food within the tract begins in one location.

❷ Segments of the digestive tract alternate between contraction and relaxation.

❸ Material in the intestine is spread out in both directions from the site of introduction.

❹ The secretion or food is spread out in the digestive tract and becomes more diffuse (*lighter color*) through time.

PROCESS Figure

PROCESS Figure 16.16 Segmental Contractions in the Small Intestine

Smooth muscle contractions in the wall of the small intestine disperse digesting food throughout its lumen.

How might reduced segmental contractions affect the digestive process?

The ileocecal sphincter at the juncture of the ileum and the large intestine remains mildly contracted most of the time, but peristaltic contractions reaching the ileocecal sphincter from the small intestine cause the sphincter to relax and allow chyme to move from the small intestine into the cecum. The ileocecal valve prevents movement from the large intestine back into the ileum.

16.6 LIVER AND PANCREAS

Learning Outcomes *After reading this section, you should be able to*

A. Describe the anatomy, histology, and ducts of the liver and pancreas.
B. Describe the major functions of the liver and pancreas
C. Explain how the liver and pancreas are regulated.

Two large accessory glands, the liver and the pancreas, produce secretions that empty into the duodenum.

Anatomy of the Liver

The **liver** is the largest internal organ of the body and weighs about 1.36 kg (3 pounds) (figure 16.17). The liver is located in the right upper quadrant of the abdomen, tucked against the inferior surface of the diaphragm. The posterior surface of the liver is in contact with right ribs 5–12. The liver consists of four lobes: (1) the **right lobe,** (2) the **left lobe** (3) the **caudate** (KAW-date; having a tail) **lobe,** and (4) the **quadrate** (KWAH-drate; square) **lobe.** The right and left lobes are separated by a connective tissue septum, called the **falciform** (FAL-si-form) **ligament.** Visible from an inferior view of the liver is the **porta** (gate), through which blood vessels, ducts, and nerves enter or exit the liver.

Figure 16.17 APR **Liver**

(*a*) Anterior view. (*b*) Inferior view. (*c*) Histology.

The liver receives blood from two sources (see chapter 13): (1) the hepatic artery and (2) the hepatic portal vein. The **hepatic** (hep-AT-ik; associated with the liver) **artery** delivers oxygenated blood to the liver, which supplies liver cells with oxygen. The **hepatic portal vein** carries

nutrient-rich blood from the digestive tract to the liver. Blood exits the liver through **hepatic veins** and empties into the inferior vena cava.

The liver is divided into **hepatic lobules.** Hepatic lobules are hexagon-shaped regions surrounded by connective tissue septa and defined by a **portal triad** at each corner and a **central vein** in the center of the lobule (figure 16.17). The portal triads are so named because three structures—(1) the hepatic portal vein, (2) the hepatic artery, and (3) the hepatic duct—are located in them. Hepatic nerves and lymphatic vessels, often too small to be seen easily in light micrographs, are also located in these areas. The central vein collects the blood as it leaves the lobule. Central veins of the lobules unite to form **hepatic veins,** which exit the liver on its posterior and superior surfaces and empty into the inferior vena cava (figure 16.17).

Hepatic cords are strings of cells that radiate out from the central vein of each lobule like the spokes of a wheel. The hepatic cords are composed of **hepatocytes,** the functional cells of the liver. Hepatocytes take up nutrients from the portal blood. The nutrients are stored, detoxified, or used to synthesize new compounds before being released into the hepatic sinusoids or into the bile canaliculi. For example, hepatocytes synthesize many plasma proteins as well as aiding in new hemoglobin synthesis by recycling iron from the degradation of old red blood cells (see figure 11.6). **Hepatic sinusoids** are blood channels in the spaces between the hepatic cords. The sinusoids are lined with a very thin, irregular squamous endothelium consisting of two cell populations: (1) extremely thin, sparse **endothelial cells** and (2) hepatic phagocytic cells. The **bile canaliculus** (kan-ah-LIK-yoo-lus; little canal) is a cleftlike lumen that lies between the cells within each cord (see figure 16.17). **Bile** produced by the hepatocytes flows through the bile canaliculi toward the hepatic triad and exits the liver through the hepatic ducts.

Figure 16.18 illustrates the flow of bile from the liver and gallbladder to where the bile joins with pancreatic secretions to empty into the duodenum.

PROCESS Figure

PROCESS Figure 16.18 APR **Flow of Bile and Pancreatic Secretions Through the Duct System of the Liver, Gallbladder, and Pancreas**

The liver produces bile, some of which is stored in the gallbladder. The bile enters the duodenum through the common bile duct.

Apply

If gallstones have formed in the gallbladder, what possible consequence could they have on secretion of bile from the gallbladder?

1. The hepatic ducts converge and empty into the right and left **hepatic ducts** to transport bile out of the liver. The right and left hepatic ducts unite to form a single **common hepatic duct.**
2. The **gallbladder** is a small sac on the inferior surface of the liver that stores concentrated bile (see figure 16.17*a*, *b*). The **cystic** (SIS-tik; *kystis,* bladder) **duct** carrying bile from the gallbladder joins the common hepatic duct to form the **common bile duct.**
3. The common bile duct joins the pancreatic duct.

4. Together they open into the duodenum at the **duodenal papilla** (pah-PILL-ah). A sphincter regulates the emptying of bile and pancreatic secretions into the duodenum.
5. Pancreatic secretions may also enter the duodenum through an accessory pancreatic duct, which also empties into the duodenum (See "Functions of the Pancreas").

Functions of the Liver

The liver plays a crucial role in metabolism and has a multitude of functions. Among other functions, the liver processes nutrients and detoxifies harmful substances from the blood. The liver also produces a fluid important for digestion, called bile (table 16.3).

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Table 16.3 Functions of the Liver

Function	Explanation
Digestion	Bile neutralizes stomach acid and emulsifies fats, which facilitates fat digestion.
Excretion	Bile contains excretory products, such as cholesterol, fats, and bile pigments (e.g., bilirubin), that result from hemoglobin breakdown.
Nutrient storage	Liver cells remove sugar from the blood and store it in the form of glycogen; they also store fat, vitamins (A, B_{12}, D, E, and K), copper, and iron.
Nutrient conversion	Liver cells convert some nutrients into others; for example, amino acids can be converted to lipids or glucose, fats can be converted to phospholipids, and vitamin D is converted to its active form.
Detoxification of harmful chemicals	Liver cells remove ammonia from the blood and convert it to urea, which is eliminated in the urine; other substances are detoxified and secreted in the bile or excreted in the urine.
Synthesis of new molecules	The liver synthesizes blood proteins, such as albumin, fibrinogen, globulins, and clotting factors.

The liver produces and secretes about 600–1000 mL of bile each day (see figure 16.2). Bile is a complex solution that contains (1) bile salts, (2) bile pigments, (3) cholesterol, (4) lipids, (5) lipid-soluble hormones, and (6) lecithin (a mixture of phospholipids). Bile contains no digestive

enzymes, but it plays a role in digestion because it neutralizes stomach acid and emulsifies lipids. The relative alkaline pH of bile helps neutralize the acidic chyme entering the duodenum. This is important because the pancreatic enzymes cannot function at the acidic pH of the chyme leaving the stomach. **Bile salts** emulsify lipids, which is necessary for subsequent digestion by lipase. Bile pigments are not required for any digestive function but instead are excretory products. Bile pigments are greenish-yellow to brown and give feces their characteristic color. One common bile pigment is **bilirubin** (bill-ee-RU-bin), which results from the breakdown of hemoglobin by hepatocytes (see chapter 11). **Gallstones** may form if the amount of cholesterol secreted by the liver becomes excessive and is not able to be dissolved by the bile salts.

Figure 16.19 describes the regulation of bile secretion and release from the gallbladder. Both neural and hormonal stimuli regulate the secretion and release of bile.

1. Parasympathetic stimulation through the vagus nerve stimulates bile secretion by the liver. Vagus nerve stimulation causes the gallbladder to contract, thereby releasing bile into the duodenum.
2. Secretin from the duodenum also stimulates bile secretion and release.
3. Cholecystokinin, also produced by the duodenum is carried through the blood to the gallbladder. There cholecystokinin stimulates the gallbladder to contract and the sphincters to relax, which releases the stored bile into the duodenum.
4. Bile salts increase bile secretion through a positive-feedback system. Over 90% of bile salts are reabsorbed in the ileum and carried in the blood by the hepatic portal circulation. Upon their return to the liver, the bile salts stimulate further bile secretion and are once again secreted into the bile. This recycling process reduces the loss of bile salts in the feces. Bile secretion into the duodenum continues until the duodenum empties.

PROCESS Figure

PROCESS Figure 16.19 **Control of Bile Secretion and Release**

Parasympathetic impulses, cholecystokinin, and secretin all stimulate bile secretion and gallbladder contractions.

What effect, if any, would cholecystokinin have on bile secretion in an individual whose gallbladder has been removed?

The liver can remove sugar from the blood and store it in the form of glycogen (table 16.3). It can also store lipids, vitamins, copper, and iron.

This storage function is usually short-term.

Our food choices (candy bars for breakfast, for example) are not always in line with the nutrient requirements of our bodies. If this is the case, the liver can convert some nutrients into others (table 16.3). For example, if a person eats a meal that is very high in protein, a large amount of amino acids and only a small amount of lipids and carbohydrates are delivered to the liver. The liver can break down the amino acids and cycle many of them through metabolic pathways to produce ATP and to synthesize lipids and glucose (see chapter 17).

The liver also transforms some nutrients into more readily usable substances. Ingested fats, for example, can be combined with choline and phosphorus in the liver to produce phospholipids, which are essential components of cell membranes.

Many ingested substances are harmful to body cells. In addition, the body itself produces many by-products of metabolism that, if accumulated, are toxic. The liver is an important line of defense against many of those harmful substances. It detoxifies them by altering their structure, which makes their excretion easier (table 16.3). For example, the liver removes ammonia, a toxic by-product of amino acid metabolism, from the blood and converts it to urea, which is then secreted into the blood and eliminated by the kidneys in the urine. The liver also removes other substances from the blood and excretes them into the bile.

The liver can also produce unique new compounds (table 16.3). Many of the blood proteins, such as albumins, fibrinogen, globulins, and clotting factors, are synthesized in the liver and released into the blood.

Anatomy of the Pancreas

The **pancreas** is a complex organ composed of both endocrine and exocrine tissues that perform several functions. The pancreas is located behind the stomach and is retroperitoneal (see figure 16.1). The **head** of the pancreas is nestled within the curvature of the duodenum (figure 16.20*a*). The body and **tail** extend to the spleen.

Figure 16.20 APR **Anatomy and Histology of the Duodenum and Pancreas**
(*a*) The head of the pancreas lies within the duodenal curvature, with the pancreatic duct emptying into the duodenum. (*b*) Histology of the pancreas, showing both the acini and the pancreatic duct system.

The endocrine part of the pancreas consists of **pancreatic islets,** or *islets of Langerhans* (figure 16.20*b*). The islet cells produce the hormones insulin and glucagon, which are very important in controlling the blood levels of nutrients, such as glucose and amino acids. The islet cells also secrete the hormone somatostatin, which regulates insulin and glucagon secretion and may inhibit growth hormone secretion (see chapter 10).

The exocrine part of the pancreas is a compound acinar gland (see chapter 4). Acinar cells within the **acini** (ASS-ih-nai; see figure 16.20*b*) produce digestive enzymes. Clusters of acini form lobules that are separated by thin septa. Exocrine secretions flow from the pancreas to the small intestine via a series of ducts, which merge to form the main **pancreatic duct** (see figure 16.20*b*). The pancreatic duct joins the common bile duct at the duodenal papilla and its secretions empty into the duodenum (figure 16.20*a;* see figure 16.18).

Functions of the Pancreas

The exocrine secretions of the pancreas include bicarbonate ions (HCO_3^-), and digestive enzymes, called pancreatic enzymes. Bicarbonate ions neutralize the acidic chyme that enters the small intestine from the stomach. The neutralized pH stops pepsin digestion. More importantly, however, the neutralized pH is required for the function of pancreatic and small intestine enzymes. The neutralized pH also prevents stomach acid from damaging the duodenum.

The pancreatic enzymes are important in digesting all major classes of food (see table 16.1). Without pancreatic enzymes, lipids, proteins, and carbohydrates cannot be adequately digested. The major protein-digesting (proteolytic) enzymes are: (1) **trypsin** (TRIP-sin), (2) **chymotrypsin** (kigh-moh-TRIP-sin), and (3) **carboxypeptidase** (kar-BOX-ee-PEP-ti-dase). The protein-digesting enzymes continue the protein digestion that started in the stomach. **Pancreatic amylase** (AM-il-eis) continues the polysaccharide digestion that began in the oral cavity. The pancreatic enzymes also include **lipase** (LIE-pase), a lipid-digesting enzyme, and **nucleases** (NOO-klee-aysez), which are enzymes that degrade DNA and RNA to their component nucleotides.

The mechanism regulating pancreatic secretion is outlined in figure 16.21. Both hormonal and neural mechanisms control the exocrine secretory activity of the pancreas (see table 16.2).

❶ Parasympathetic stimulation from the vagus nerve causes the pancreas to release a secretion rich in digestive enzymes. Conversely, sympathetic action potentials inhibit pancreatic secretion.

❷ Acidic chyme in the duodenum stimulates secretin release. In turn, secretin stimulates the pancreas to release a watery secretion, rich in HCO_3^- into the duodenum.

❸ Fatty acids and amino acids in the duodenum stimulate cholecystokinin release. In turn, cholecystokinin stimulates the pancreas to release an enzyme-rich solution. These pancreatic enzymes digest the fatty acids and amino acids.

PROCESS Figure

PROCESS Figure 16.21 **Control of Pancreatic Secretion**

Cholecystokinin and parasympathetic impulses stimulate pancreatic enzyme secretion. Secretin stimulates secretion of bicarbonate from the pancreas.

Blockage of the pancreatic duct prevents pancreatic enzymes from being delivered to the small intestine. What effect would you expect this to have on cholecystokinin and secretin levels in the blood?

Apply It 3

Explain how secretin production in response to acidic chyme and bicarbonate ion secretion in response to secretin constitute a negative-feedback mechanism.

16.7 LARGE INTESTINE

Learning Outcomes *After reading this section, you should be able to*

A. List the parts of the large intestine.
B. Describe the anatomy and the histology of the large intestine.
C. Describe the major functions of the large intestine.
D. Explain how movement in the large intestine is regulated.

Anatomy of the Large Intestine

The **large intestine** is the portion of the digestive tract extending from the ileocecal junction to the anus (see figure 16.2). It consists of four parts: (1) cecum, (2) colon, (3) rectum, and (4) anal canal. Normally, 18–24 hours are required for material to pass through the large intestine, in contrast to the 3–5 hours required for chyme to move through the small intestine. Thus, the movements of the colon are more sluggish than those of the small intestine. While in the colon, chyme is converted to **feces** (FEE-sees). The colon stores the feces until they are eliminated by defecation. About 1500 mL of chyme enter the cecum each day, but more than 90% of the volume is reabsorbed, so that only 80–150 mL of feces are normally eliminated by defecation.

Cecum

The **cecum** (SEE-kum) is the proximal end of the large intestine where it joins with the small intestine at the ileocecal junction. The cecum is located in the right lower quadrant of the abdomen near the iliac fossa. The cecum is a sac that extends inferiorly about 6 cm past the ileocecal junction. Attached to the cecum is a tube about 9 cm long called the **appendix.** The walls of the appendix contain many lymphatic nodules, which contribute to immune functions.

Appendicitis is an inflammation of the appendix that usually occurs because of an obstruction. Secretions from the appendix cannot pass the obstruction; therefore, they accumulate, causing enlargement and pain. Bacteria around the appendix can cause infection. Symptoms include sudden abdominal pain, particularly in the right lower quadrant at a specific point called the McBurney point. The McBurney point is midway between the umbilicus and the right superior iliac spine of the hip bone. Appendicitis also can cause a slight fever, loss of appetite, constipation or diarrhea, nausea, and vomiting. If the appendix bursts, the infection can spread throughout the peritoneal cavity, causing peritonitis with life-threatening results. Each year, 500,000 people in the United States suffer

from appendicitis. The usual treatment is an appendectomy, surgical removal of the appendix.

Colon

The **colon** (KOH-lon) is about 1.5–1.8 m long and consists of four parts: (1) the ascending colon, (2) the transverse colon, (3) the descending colon, and (4) the sigmoid colon (figure 16.22). The **ascending colon** extends superiorly from the cecum to the right colic flexure, near the liver, where the colon turns to the left. The **transverse colon** extends from the right colic flexure to the left colic flexure near the spleen, where the colon turns inferiorly; and the **descending colon** extends from the left colic flexure to the pelvis, where the colon becomes the **sigmoid colon.** The sigmoid colon forms an S-shaped tube that extends medially and then inferiorly into the pelvic cavity and ends at the rectum.

Figure 16.22 APR **Large Intestine**

(*a*) The large intestine consists of the cecum, colon, rectum, and anal canal. The teniae coli are bands of smooth muscle along the length of the colon. (*b*) Radiograph of the large intestine following a barium enema.

(b) ©CNRI/SPL/Science Source

The mucosal lining of the colon contains numerous straight, tubular glands called **crypts,** which contain many mucus-producing goblet cells. The longitudinal smooth muscle layer of the colon does not completely

envelop the intestinal wall but forms three bands called **teniae coli** (TEE-nee-aye KOH-lye).

Rectum

The **rectum** is a straight, muscular tube that begins at the termination of the sigmoid colon and ends at the anal canal (figure 16.22). The muscular tunic is composed of smooth muscle and is relatively thick in the rectum compared to the rest of the digestive tract.

Anal Canal

The last 2–3 cm of the digestive tract is the **anal canal.** It begins at the inferior end of the rectum and ends at the **anus** (external digestive tract opening). The smooth muscle layer of the anal canal is even thicker than that of the rectum and forms the **internal anal sphincter** at its superior end. The **external anal sphincter** at the inferior end of the anal canal is formed by skeletal muscle.

Hemorrhoids are enlarged or inflamed rectal, or hemorrhoidal, veins that supply the anal canal. Hemorrhoids may cause pain, itching, and/or bleeding around the anus. They can usually be treated by changes in diet or medications.

Functions of the Large Intestine

Feces formation in the colon is due to the absorption of water and salts, the secretion of mucus, and extensive action of microorganisms. The colon stores the feces until they are eliminated by the process of **defecation** (def-eh-KAY-shun).

Numerous microorganisms inhabit the colon. They reproduce rapidly and ultimately constitute about 30% of the dry weight of the feces. Some bacteria in the intestine synthesize vitamin K and other vitamins, which are passively absorbed in the colon.

Every 8–12 hours, large parts of the colon undergo several strong contractions, called **mass movements,** which propel the colon contents a considerable distance toward the anus. Each mass movement contraction extends over 20 or more centimeters of the large intestine, which is a much longer part of the digestive tract than that covered by a peristaltic contraction. These mass movements are very common following some meals, especially breakfast.

During defecation, the contractions that move feces toward the anus must be coordinated with the relaxation of the internal and external anal

sphincters. The movement of feces from the colon into the rectum distends the rectal wall, which stimulates the defecation reflex. The **defecation reflex** consists of local and parasympathetic reflexes. Local reflexes cause weak contractions of the distal colon and rectum and relaxation of the internal anal sphincter. Parasympathetic reflexes are responsible for most of the defecation reflex. Action potentials produced in response to distension of the rectal wall travel along sensory nerve fibers to the defecation reflex center of the spinal cord. Then motor action potentials are initiated that return through nerves to the colon and rectum, reinforcing peristaltic contractions and relaxation of the internal anal sphincter.

The internal and external anal sphincters prevent defecation. Resting sphincter pressure results from tonic muscle contractions, mostly of the internal anal sphincter. In response to increased abdominal pressure, reflexes mediated through the spinal cord cause contractions of the external anal sphincter. Thus, the untimely expulsion of feces during coughing or exertion is avoided.

There is also conscious control of the defecation reflex. Action potentials from the spinal cord ascend to the brain, where parts of the brainstem and hypothalamus inhibit or facilitate reflex activity in the spinal cord. In addition, action potentials ascend to the cerebrum, where awareness of the need to defecate is realized. The external anal sphincter is composed of skeletal muscle and is under conscious cerebral control. If this sphincter is relaxed voluntarily, feces are expelled. On the other hand, increased contraction of the external anal sphincter prevents defecation. The defecation reflex persists for only a few minutes and quickly declines. Generally, the reflex is re-initiated after a period that may be as long as several hours. Mass movements in the colon are usually the reason for re-initiation of the defecation reflex.

Defecation can be initiated by voluntary actions that stimulate a defecation reflex. This “straining” includes a large inspiration of air, followed by closure of the larynx and forceful contraction of the abdominal muscles. As a consequence, the pressure in the abdominal cavity increases and forces feces into the rectum. Stretch of the rectum initiates a defecation reflex, and input from the brain overrides the reflexive contraction of the external anal sphincter stimulated by increased abdominal pressure. The increased abdominal pressure also helps push feces through the rectum.

Apply It 4

Explain how inserting liquid or gas into the rectum during a procedure called an enema stimulates defecation.

16.8 DIGESTION, ABSORPTION, AND TRANSPORT

Learning Outcomes *After reading this section, you should be able to*

A. Describe the digestion, absorption, and transport of carbohydrates, proteins, vitamins, and minerals.

B. Describe the digestion, absorption, and transport of fats and lipids.

C. Discuss water movement into and out of the digestive tract.

Digestion is the breakdown of food to molecules that are small enough to be absorbed into the blood. There are two types of digestion: (1) mechanical digestion and (2) chemical digestion. **Mechanical digestion** breaks large food particles into smaller ones. **Chemical digestion** uses enzymes to break covalent chemical bonds in organic molecules. Large organic molecules are broken down into smaller molecules. Specifically, carbohydrates are broken down into monosaccharides, lipids get broken down into fatty acids and monoglycerides, and proteins get broken down into amino acids (figure 16.23).

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Figure 16.23 **Digestion**

Food consists primarily of carbohydrates, lipids, and proteins. Carbohydrates are broken down into monosaccharides, lipids into fatty acids and monoglycerides, and proteins into amino acids.

Absorption begins in the stomach, where some small, lipid-soluble molecules, such as alcohol and aspirin, can diffuse through the stomach epithelium into the blood. Most absorption occurs in the duodenum and jejunum, although some occurs in the ileum. Some molecules can diffuse through the intestinal wall, whereas others must be transported across the intestinal wall. **Transport** requires carrier molecules and includes facilitated diffusion, cotransport, and active transport. Cotransport and active transport require energy to move the transported molecules across the intestinal wall.

Carbohydrates

Ingested **carbohydrates** (kar-boh-HIGH-drates) consist primarily of starches, cellulose, sucrose (table sugar), and small amounts of fructose (fruit sugar) and lactose (milk sugar). Starches, cellulose, sucrose, and fructose are derived from plants, and lactose is derived from animals. **Polysaccharides** (pol-ee-SACK-ah-rides) are large carbohydrates, such as starches, cellulose, and glycogen, that consist of many sugars linked by chemical bonds. Starch is an energy-storage molecule in plants. Cellulose forms the walls of plant cells. Glycogen is an energy-storage molecule in animals and is contained in muscle and in the liver. When uncooked meats are processed or stored, the glycogen is broken down to glucose, which is further broken down, so that little, if any, glycogen remains. Therefore, almost all dietary carbohydrates come from plants. Starch is broken down by enzymes. Cellulose is a polysaccharide that is not digested but is important for providing fiber in the diet.

Salivary amylase begins the digestion of carbohydrates in the mouth (figure 16.24). The carbohydrates then pass to the stomach, where digestion continues until the food is well mixed with acid, which inactivates salivary amylase. Carbohydrate digestion is resumed in the duodenum by **pancreatic amylase.** Salivary and pancreatic amylase break down polysaccharides into the smaller **disaccharides** (die-SACK-ah-rides; two sugars see chapter 2). However, disaccharides cannot be absorbed and must be further broken down so that carbohydrate absorption can occur.

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Oral Cavity

Salivary amylase:

Complex carbohydrates → **Polysaccharides and Disaccharides**

Stomach

Pepsin:

Proteins → **Polypeptides**

Figure 16.24 **Digestion of Carbohydrates, Lipids, and Proteins**
The enzymes involved in digesting carbohydrates, lipids, and proteins are depicted in relation to the region of the digestive tract where each functions.

The final step in carbohydrate digestion is performed by **disaccharidases,** a group of enzymes bound to the intestinal epithelium. These enzymes digest disaccharides into several types of monosaccharides, including glucose, the major monosaccharide used by humans. For example, one disaccharidase is lactase, which breaks down lactose (milk sugar). Many people have heard of lactase, because lack of it leads to lactose intolerance. Lactase is made at birth; however, in 5–15% of the European-American population and 80–90% of the African-American and Asian-American populations, lactase synthesis sharply declines 3–4 years after weaning. In the absence of lactase, ingestion of dairy products causes intestinal cramping, bloating, and diarrhea. An increasing selection of foods for lactose-intolerant people can be found in the supermarket. This information may help you answer this chapter's Learn to Apply It question.

The **monosaccharides** (MON-oh-SACK-ah-rides; single sugars) glucose, galactose, and fructose are absorbed by intestinal epithelial cells.

Recall from chapter 3 that certain molecules are transported across the cell membrane by proteins called carrier molecules. In cotransport, one carrier molecule can move two molecules in the same direction into or out of a cell. Absorption of the monosaccharides, glucose, and galactose occurs through cotransport. The sodium-potassium pump establishes a Na^+ concentration gradient. Diffusion of Na^+ down its concentration gradient provides the energy to transport glucose across the cell membrane. In chapter 3 you learned that this process is called secondary active transport. In contrast to glucose and galactose, the monosaccharide fructose is absorbed through the process of facilitated diffusion, which also uses a carrier molecule. As an example of cotransport, figure 16.25 outlines the process of glucose transport.

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PROCESS Figure

PROCESS Figure 16.25 **Transport of Glucose Across the Intestinal Epithelium**

Glucose absorption occurs through cotransport.

If a drug is given that inhibits the Na^+/K^+ pump, specifically in intestinal epithelial cells, how will glucose absorption be affected?

1. Glucose is absorbed by cotransport with Na^+ into intestinal epithelial cells.
2. Cotransport is driven by a sodium gradient established by a Na^+–K^+ pump.
3. Glucose moves out of the intestinal epithelial cells by facilitated diffusion.
4. Glucose enters the capillaries of the intestinal villi and is carried through the hepatic portal vein to the liver.

Liver cells convert different types of monosaccharides to **glucose,** which then leaves the liver via the blood to be distributed throughout the body. Glucose enters body cells by facilitated diffusion. The rate of glucose transport into most types of cells is greatly influenced by **insulin** and can increase tenfold in the presence of insulin. Without insulin, such as can be the case in diabetes mellitus, glucose enters most cells very slowly (see chapter 10).

Lipids

Lipid molecules are insoluble or only slightly soluble in water (see chapter 2). Lipids include triglycerides, phospholipids, steroids, and fat-soluble vitamins. **Triglycerides** (trie-GLISS-eh-ridez), or fats, are the most common type of lipid. They consist of three fatty acids bound to glycerol. **Saturated** fats have only single bonds between carbons of the fatty acids. **Unsaturated** fats have double bonds between carbons of the fatty acids (see chapter 2). Saturated fats are solid at room temperature and are found in meat, dairy products, eggs, nuts, and certain oils such as coconut oil and palm oil. Unsaturated fats are liquid at room temperature and are found in fish and most plant-based oils.

Lipase, secreted by the pancreas, digests lipid molecules (see figure 16.24). The primary products of this digestive process are fatty acids and monoglycerides. However, the lipases alone cannot efficiently digest lipids.

A key step in lipid digestion is **emulsification** (ih-MUL-see-fi-ca-shun), by which bile salts transform large lipid droplets into much smaller lipid droplets. The bile salts mix with lipids and act as detergents to disrupt lipid droplets. By decreasing the droplet size and increasing the droplet number, the emulsification process increases the surface area of the lipid droplets exposed to the digestive enzymes. This is necessary because the lipases are water-soluble and can digest lipids only at the surface of the lipid droplets. Try performing some of your own emulsification. First, mix some cooking oil and food coloring. After shaking or stirring, does the food coloring mix well with the oil? Now, to emulsify the cooking oil, add a drop or two of dish detergent and shake or stir again. Does the food coloring mix with the oil better than before?

Figure 16.26 illustrates the process by which lipids are absorbed.

PROCESS Figure

PROCESS Figure 16.26 **Transport of Lipids Across the Intestinal Epithelium**

Lipid absorption occurs when micelles enter intestinal epithelial cells.

Why must digested lipids be moved by exocytosis out of the intestinal epithelial cells into lacteals of the lymphatic system?

1. Once lipids are digested in the intestine, bile salts aggregate around the small droplets of digested lipids to form **micelles** (mi-SELZ, my-SEL; small morsels). The hydrophobic (water-fearing) ends of the bile salts are directed toward the lipid particles, and the hydrophilic (water-loving) ends are directed outward, toward the water environment.
2. When a micelle comes in contact with the epithelial cells of the small intestine, the lipids, fatty acids, and monoglyceride molecules pass, by simple diffusion, from the micelles through the cell membranes of the epithelial cells.
3. Once inside the intestinal epithelial cells, the fatty acids and monoglycerides are recombined to form triglycerides. These, and other lipids, are packaged inside a protein coat. The packaged lipid-protein complexes, or **lipoproteins,** are called **chylomicrons** (kye-lo-MY-kronz).
4. Chylomicrons leave the epithelial cells via exocytosis and enter the lacteals, lymphatic capillaries within the intestinal villi. Lymph containing large amounts of absorbed lipid is called **chyle** (KILE; milky lymph). The lymphatic system carries the chyle to the bloodstream.

Chylomicrons are then transported to the liver. There are three possible fates for lipids in the liver: (1) the lipids can be stored, (2) the lipids can be converted into other molecules, or (3) the lipids can be used as energy. The lipids are also transported to adipose tissue, where they are stored until needed by body. Other lipoproteins, called **low-density lipoproteins (LDLs)** and **high-density lipoproteins (HDLs),** transport cholesterol and fat in the blood (figure 16.27). LDLs carry cholesterol to the tissues for use by the cells. HDLs transport cholesterol from the tissues to the liver.

Figure 16.27 **Lipoproteins**

Cholesterol and fat are transported through the blood by lipoproteins.

Proteins

Proteins are chains of **amino acids.** They are found in most of the plant and animal products we eat. **Pepsin** is a protein-digesting enzyme secreted by the stomach. Pepsin breaks down large proteins into smaller, individual **polypeptides** (see figure 16.24). Pepsin digests only about 10–20% of the total ingested protein. In the small intestine, the enzymes **trypsin, chymotrypsin,** and **carboxypeptidase** continue protein digestion. These enzymes are synthesized by the pancreas in an inactive state. Once they are in the small intestine, these enzymes are activated. In the small intestine, other enzymes called **peptidases** further break down small peptides into tripeptides (three amino acids), dipeptides (two amino acids), or single amino acids. The peptidases are bound to the microvilli of the small intestine.

MICROBES IN YOUR BODY

Fecal Transplants

Would you be shocked if your doctor said that the one thing that could save your life was feces? Unfortunately, we are in the midst of a global, hospital-acquired diarrhea epidemic. The cause of this epidemic is a bacterium called *Clostridium difficile* (commonly referred to as *C. diff*), a pathogen that is normally found in the colon, but is controlled by the normal microbiota. One of the most critical functions of the normal gut microbiota is prevention of infections through competition with pathogens. As a consequence, when a patient takes antibiotics, *C. diff* can flourish and cause life-threatening diarrhea. Treatment of *C. diff* infections with specific antibiotics will often stop the diarrhea initially. However, *C. diff* are spore-forming bacteria. Spores are very stable structures that allow bacteria to withstand harsh conditions until favorable conditions return and the bacteria can regrow. Thus, antibiotics kill only the *C. diff* cells, not the spores. Hence, it is very common for patients to suffer multiple recurrences of diarrhea for months, which can lead to death in some patients. Additionally, a more virulent, resistant strain of *C. diff* has emerged. This strain is resistant to certain antibiotics and makes a greater number of spores and more of the toxins responsible for the diarrhea.

So, where do feces come into play? Because antibiotic treatments are not effective (65% infection recurrence), physicians are considering an old treatment: fecal transplants. The first documented case of transplanting feces from a healthy donor into a diseased recipient was in 1958. Fecal transplantation has since been used successfully in veterinary medicine for decades. However, due to the unappealing nature of this treatment, it has only recently been considered an option in humans. Now more commonly known as intestinal fecal transplantation (IFT), it has been shown to effectively treat diarrhea in over 90% of *C. diff* infections. The idea is that a healthy donor—usually a close family household member such as a spouse or significant partner—donates their feces. The feces are mixed with physiological saline, filtered, and then introduced into the recipient's gastrointestinal (GI) tract by one of two ways: the upper GI tract route or the lower GI tract route. The upper GI tract route uses either a gastroscope or nasogastric tube to transfer the material to the recipient's intestine. Of the two, this one is easier and costs less. However, there is the possibility the donor microbiota may not reach the end of the colon or that the patient may vomit the fecal material. The lower GI tract route uses a colonoscope or enema and is the preferred approach, but does run the risk of perforating the colon. Thus, as of yet, there is no standardized method for transferring the donor feces. However, research is showing that more and more patients may overcome their initial reluctance when presented with a predictable success rate and greater reliability than other protocols. In addition, the recent "RePOOPulating" study shows promise that doctors may soon be able to treat *C. diff* infections simply by prescribing a pill that contains normal microbiota.[1]

[1]Source: Petrof, E.O. et al, *Stool substitute transplant therapy for the eradication of Clostridium difficile infection: 'RePOOPulating' the gut*. Microbiome, 2013, 1-3.

Figure 16.28 outlines the process of amino acid absorption.

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PROCESS Figure

PROCESS Figure 16.28 Transport of Amino Acids Across the Intestinal Epithelium

Amino acid absorption occurs through cotransport.

Why is it beneficial to transport absorbed amino acids to the liver?

❶ Absorption of tripeptides, dipeptides, or individual amino acids occurs through the intestinal epithelial cells by various cotransport mechanisms.

❷ Many, but not all, amino acids are absorbed by cotransport with a Na^+ gradient, similar to the mechanism used for glucose transport. Within the intestinal epithelial cells, tripeptides and dipeptides are broken down into amino acids.

❸ Next, the amino acids move out of the intestinal epithelial cells.

❹ The amino acids then enter blood capillaries in the villi and are carried by the hepatic portal vein to the liver. The amino acids may be modified in the liver, or they may be released into the blood and distributed throughout the body.

Amino acids are actively transported into the various cells of the body. This transport is stimulated by growth hormone and insulin. Most amino acids are used as building blocks to form new proteins (see chapter 2), but some may be metabolized, with a portion of the released energy used to produce ATP. The body cannot store excess amino acids. Instead, they are partially broken down and used to synthesize glycogen or lipids, which can be stored. The body can store only small amounts of glycogen, so most of the excess amino acids are converted to lipids.

Water and Minerals

Approximately 9 L of water enter the digestive tract each day (figure 16.29). We ingest about 2 L in food and drink, and the remaining 7 L are from digestive secretions. Approximately 92% of that water is absorbed in the small intestine, about 7% is absorbed in the large intestine, and about 1% leaves the body in the feces. Water can move in either direction by osmosis across the wall of the digestive tract. The direction of water movement is determined by osmotic gradients across the epithelium. When the chyme is dilute, water moves out of the intestine into the blood. If the chyme is concentrated, water moves out of the blood into the small intestine.

Figure 16.29 **Fluid Volumes in the Digestive Tract**

Fluid movement across the digestive tract varies depending on the particular segment.

Sodium, potassium, calcium, magnesium, and phosphate ions are actively transported from the small intestine. Vitamin D is required for the transport of Ca^{2+}. Negatively charged Cl^- moves passively through the wall of the duodenum and jejunum with the positively charged Na^+, but Cl^- is actively transported from the ileum.

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SYSTEMS PATHOLOGY

Diarrhea

Background Information

Diarrhea is one of the most common complaints in clinical medicine (figure 16.30). Diarrhea affects more than half the tourists in developing countries (figure 16.31), where it may result from eating food to which the digestive tract is not accustomed or from ingesting food or water contaminated with pathogens.

Figure 16.30 Effects of Diarrhea on Other Body Systems

Diarrhea affects many systems of the body, as this diagram illustrates.

Figure 16.31 Many Tourists Develop Diarrhea

Ingesting food and drink in a foreign locale can cause gastrointestinal upset.

©Juice Images/Alamy RF

Diarrhea is any change in bowel habits involving increased stool frequency or volume or increased stool fluidity. It is not a disease in itself, but it can be a symptom of a wide variety of disorders. Diarrhea that lasts less than 2–3 weeks is acute diarrhea; diarrhea lasting longer is considered chronic. Acute diarrhea is usually self-limiting, but some forms of diarrhea can be fatal if not treated. Diarrhea results from either a decrease in fluid absorption in the intestine or an increase in fluid secretion. It can also be caused by increased bowel motility that moves chyme rapidly through the small intestine, so that more water enters the colon.

Mucus secretion increases dramatically in response to diarrhea. This mucus contains large quantities of bicarbonate ions, which enter the mucus. This can result in a condition called metabolic acidosis (see chapter 18).

Diarrhea is usually caused by bacteria, viruses, amoebic parasites, or chemical toxins. Symptoms can begin from as little as 1–2 hours after bacterial toxins are ingested to as long as 24 hours or more for some strains of bacteria. Some types of bacterial diarrhea are associated with severe vomiting, whereas others are not. Identifying the causal organism usually requires laboratory analysis of the food or stool, but in cases of acute diarrhea, the infectious agent is seldom identified.

Table 16.4 REPRESENTATIVE DISEASES AND DISORDERS: Digestive System

Condition	Description
Stomach	
Peptic ulcer	Lesions in the lining of the stomach or duodenum, usually due to infection by the bacterium *Helicobacter pylori*; stress, diet, smoking, or alcohol may be predisposing factors; antibiotic therapy is the accepted treatment
Liver	
Cirrhosis (sir-OH-sis)	Characterized by damage to and death of hepatic cells and replacement by connective tissue; results in loss of normal liver function and interference with blood flow through the liver; a common consequence of alcoholism
Hepatitis (hep-ah-TYE-tis)	Inflammation of the liver that causes liver cell death and replacement by scar tissue; if not corrected, results in loss of liver function and eventually death; symptoms include nausea, abdominal pain, fever, chills, malaise, and jaundice; caused by any of seven distinct viruses
Hepatitis A	Infectious hepatitis; usually transmitted by poor sanitation practices or from mollusks living in contaminated waters

Condition	Description
Hepatitis B	Serum hepatitis; usually transmitted through blood or other body fluids through either sexual contact or contaminated hypodermic needles
Hepatitis C	Often a chronic disease leading to cirrhosis and possibly cancer of the liver
Intestine	
Inflammatory bowel disease (IBD)	Localized inflammatory degeneration that may occur anywhere along the digestive tract but most commonly involves the distal ileum and proximal colon; the intestinal wall often becomes thickened, constricting the lumen, with ulcers and fissures in the damaged areas; symptoms include diarrhea, abdominal pain, fever, fatigue, and weight loss; cause is unknown; treatments involve anti-inflammatory drugs, avoidance of foods that produce symptoms, and surgery in some cases; also called Crohn's disease or ulcerative colitis
Irritable bowel syndrome (IBS)	Disorder of unknown cause marked by alternating bouts of constipation and diarrhea; may be linked to stress or depression; high familial incidence
Gluten enteropathy (celiac disease)	Malabsorption in the small intestine due to the effects of gluten, a protein in certain grains, especially wheat; the reaction can destroy newly formed epithelial cells, causing the intestinal villi to become blunted and decreasing the intestinal surface, which reduces absorption of nutrients
Constipation (kon-sti-PAY-shun)	Slow movement of feces through the large intestine, causing the feces to become dry and hard because of increased fluid absorption while being retained; often results from inhibiting normal defecation reflexes; spasms of the sigmoid colon resulting from irritation can also result in slow feces movement and constipation; high-fiber diet can be preventative
INFECTIONS OF THE DIGESTIVE TRACT	
Food poisoning	Caused by ingesting bacteria or toxins, such as *Staphylococcus aureus, Salmonella,* or *Escherichia coli*; symptoms include nausea, abdominal pain, vomiting, and diarrhea; in severe cases, death can occur
Giardiasis (jee-ar-DYE-a-sis)	Caused by a protozoan, *Giardia lamblia*, that invades the intestine; symptoms include nausea, abdominal cramps, weakness, weight loss, and malaise; bacteria are transmitted in the feces of humans and other animals, often by drinking from contaminated wilderness streams

Condition	Description
Intestinal parasites	Common under conditions of poor sanitation; parasites include tapeworms, pinworms, hookworms, and roundworms
Dysentery (DIS-en-tair-ee)	Severe form of diarrhea with blood or mucus in the feces; can be caused by bacteria, protozoa, or amoebae

Treatment of diarrhea involves replacing lost fluids and ions. Medicines that may help combat diarrhea increase mucus and HCO_3^- secretion, decrease pepsin activity, and slow intestinal motility. Patients should avoid milk and milk products. A normal diet can be resumed after 2–3 days.

Apply It 5

Explain the effects of prolonged diarrhea on the cardiovascular system.

As a person ages, the connective tissue layers of the digestive tract—the submucosa and serosa—tend to thin. The blood supply to the digestive tract decreases. There is also a decrease in the number of smooth muscle cells in the muscularis, resulting in decreased motility in the digestive tract. In addition, goblet cells within the mucosa secrete less mucus. Glands along the digestive tract, such as the gastric glands, the liver, and the pancreas, also tend to secrete less with age. However, these changes by themselves don't appreciably decrease the function of the digestive system.

Through the years, the digestive tract, like the skin and lungs, is directly exposed to materials from the outside environment. Some of those substances can cause mechanical damage to the digestive tract, and others may be toxic to the tissues. Because the connective tissue of the digestive tract becomes thin with age and because the protective mucous covering is reduced, the digestive tract of elderly people becomes less and less protected

from these outside influences. In addition, the mucosa of elderly people tends to heal more slowly following injury. The liver's ability to detoxify certain chemicals tends to decline; the ability of the hepatic phagocytic cells to remove particulate contaminants decreases; and the liver's ability to store glycogen decreases.

This overall decline in the defenses of the digestive tract leaves elderly people more susceptible to infections and to the effects of toxic agents. Elderly people are more likely to develop ulcerations and cancers of the digestive tract. Colorectal cancers, for example, are the second leading cause of cancer deaths in the United States, with an estimated 135,000 new cases and 57,000 deaths each year.

Gastroesophageal reflux disorder (GERD) increases with advancing age. It is probably the main reason that elderly people take antacids and inhibitors of hydrochloric acid secretion. Disorders that are not necessarily age-induced, such as hiatal hernia and irregular or inadequate esophageal motility, may be worsened by the effects of aging, because of general decreased motility in the digestive tract.

The enamel on the surface of elderly people's teeth becomes thinner with age and may expose the underlying dentin. In addition, the gingiva covering the tooth root recedes, exposing additional dentin. Exposed dentin may become painful and change the person's eating habits. Many elderly people also lose teeth, which can have a marked effect on eating habits unless artificial teeth are provided. The muscles of mastication tend to become weaker; as a result, older people tend to chew their food less before swallowing.

SUMMARY

16.1 Functions of the Digestive System

The functions of the digestive system are to take in food, break down the food, absorb the digested molecules, provide nutrients to the body, and eliminate wastes.

16.2 Anatomy and Histology of the Digestive System

The digestive tract is composed of four tunics: the mucosa, the submucosa, the muscularis, and a serosa or an adventitia.

16.3 Oral Cavity, Pharynx, and Esophagus

Anatomy of the Oral Cavity

1. The lips and cheeks are involved in mastication and speech.
2. The tongue is involved in speech, taste, mastication, and swallowing.
3. There are 32 permanent teeth, including incisors, canines, premolars, and molars. Each tooth consists of a crown, a neck, and a root.
4. The roof of the oral cavity is divided into the hard and soft palates.
5. Salivary glands produce serous and mucous secretions. The three major pairs of large salivary glands are the parotid, submandibular, and sublingual glands.

Saliva

Saliva helps protect the mouth from oral bacteria, starts starch digestion, and provides lubrication.

Mastication

Mastication is accomplished by the teeth, which cut, tear, and crush the food.

Pharynx

The pharynx consists of the nasopharynx, oropharynx, and laryngopharynx.

Esophagus

The esophagus connects the pharynx to the stomach. The upper and lower esophageal sphincters regulate movement.

Swallowing

1. During the voluntary phase of swallowing, a bolus of food is moved by the tongue from the oral cavity to the pharynx.
2. During the pharyngeal phase of swallowing, the soft palate closes the nasopharynx, and the epiglottis closes the opening into the larynx. Pharyngeal muscles elevate the pharynx and larynx and then move the bolus to the esophagus.
3. During the esophageal phase of swallowing, a wave of constriction (peristalsis) moves the food down the esophagus to the stomach.

16.4 Stomach

Anatomy of the Stomach

1. The stomach connects to the esophagus at the gastroesophageal opening and to the duodenum at the pyloric opening.
2. The wall of the stomach consists of three muscle layers: longitudinal, circular, and oblique.
3. Gastric glands contain mucous neck cells, parietal cells, endocrine cells, and chief cells.

Secretions of the Stomach

1. Mucus protects the stomach lining.
2. Hydrochloric acid kills microorganisms and activates pepsin.
3. Pepsin starts protein digestion.
4. Intrinsic factor aids in vitamin B12 absorption.

Regulation of Stomach Secretions

1. Parasympathetic stimulation, gastrin, and histamine increase stomach secretions.
2. During the cephalic phase, the stomach secretions are initiated by the sight, smell, taste, or thought of food.
3. During the gastric phase, partially digested proteins and distention of the stomach promote secretion.

4. During the intestinal phase, acidic chyme in the duodenum stimulates neuronal reflexes and the secretion of hormones that inhibit gastric secretions by negative-feedback loops. Secretin and cholecystokinin inhibit gastric secretion.

Movement in the Stomach

1. Mixing waves mix the stomach contents with the stomach secretions to form chyme.
2. Peristaltic waves move the chyme into the duodenum. Increased motility increases emptying.
3. Distention of the stomach increases gastric motility. Neural and hormonal feedback loops from the duodenum inhibit gastric motility. Cholecystokinin is a major inhibitor of gastric motility.

16.5 Small Intestine

Anatomy of the Small Intestine

1. The small intestine is divided into the duodenum, jejunum, and ileum.
2. Circular folds, villi, and microvilli greatly increase the surface area of the intestinal lining.
3. Goblet cells and duodenal glands produce mucus.

Secretions of the Small Intestine

1. Mucus protects against digestive enzymes and stomach acids.
2. Chemical or tactile irritation, vagal stimulation, and secretin stimulate intestinal secretion.

Movement in the Small Intestine

1. Peristaltic contractions occur over the length of the intestine and propel chyme through the intestine.
2. Segmental contractions occur over short distances and mix the intestinal contents.

16.6 Liver and Pancreas

Anatomy of the Liver

1. The liver consists of four lobes. It receives blood from the hepatic artery and the hepatic portal vein.
2. Branches of the hepatic artery and hepatic portal vein empty into hepatic sinusoids, which empty into a central vein in the center of each lobe. The central veins empty into hepatic veins, which exit the liver.
3. The liver is divided into lobules with portal triads at the corners. Portal triads contain branches of the hepatic portal vein, hepatic artery, and hepatic duct.

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4. Hepatic cords, formed by hepatocytes, form the substance of each lobule. A bile canaliculus, between the cells of each cord, joins the hepatic duct system.
5. Bile leaves the liver through the hepatic duct system. The right and left hepatic ducts join to form the common hepatic duct. The gallbladder stores bile. The cystic duct joins the common hepatic duct to form the common bile duct. The common bile duct joins the pancreatic duct and empties into the duodenum.

Functions of the Liver

1. The liver produces bile, which contains bile salts that emulsify fats, and excretory products.
2. The liver stores and processes nutrients, produces new molecules, and detoxifies molecules.

Anatomy of the Pancreas

The pancreas is both an endocrine and an exocrine gland. Its endocrine function is to control blood nutrient levels. Its exocrine function is to produce bicarbonate ions and digestive enzymes.

Functions of the Pancreas

1. The pancreas produces HCO_3^- and digestive enzymes.
2. Acidic chyme stimulates the release of a watery bicarbonate solution that neutralizes acidic chyme. Fatty acids and amino acids in the duodenum stimulate the release of pancreatic enzymes.

16.7 Large Intestine

Anatomy of the Large Intestine

1. The cecum forms a blind sac at the junction of the small and large intestines. The appendix is a blind sac off the cecum.
2. The colon consists of ascending, transverse, descending, and sigmoid portions.
3. The large intestine contains mucus-producing crypts.
4. The rectum is a straight tube that ends at the anal canal.
5. The anal canal is surrounded by an internal anal sphincter (smooth muscle) and an external anal sphincter (skeletal muscle).

Functions of the Large Intestine

1. The functions of the large intestine are feces production and water absorption.
2. Mass movements occur three or four times a day.
3. Defecation is the elimination of feces. Reflex activity moves feces through the internal anal sphincter. Voluntary activity regulates movement through the external anal sphincter.

16.8 Digestion, Absorption, and Transport

Digestion is the chemical breakdown of organic molecules into their component parts. After the molecules are digested, some diffuse through the intestinal wall; others must be transported across the intestinal wall.

Carbohydrates

1. Polysaccharides are split into disaccharides by salivary and pancreatic amylases.
2. Disaccharides are broken down to monosaccharides by disaccharidases on the surface of the intestinal epithelium.
3. The major monosaccharide, glucose, is absorbed by cotransport with Na+ into intestinal epithelial cells. The transport is driven by the Na+ gradient generated by the sodium-potassium pump.

4. Glucose is carried by the hepatic portal vein to the liver and enters most cells in the body by facilitated diffusion. Insulin increases the rate of glucose transport into most cells.

Lipids

1. Bile salts emulsify lipids.
2. Lipase breaks down lipids. The breakdown products aggregate with bile salts to form micelles.
3. Micelles come in contact with the intestinal epithelium, and their contents diffuse into the cells, where they are packaged and released into the lacteals.

Peritoneum

1. The peritoneum is a serous membrane that lines the abdominal cavity and covers the organs.
2. Mesenteries are double layers of peritoneum that extend from the body wall to many of the abdominal organs.
3. Retroperitoneal organs are located behind the parietal peritoneum.
4. Lipids are stored in adipose tissue and in the liver, both of which release the lipids into the blood when energy sources are needed elsewhere in the body.

Proteins

1. Proteins are split into small polypeptides by enzymes secreted by the stomach and pancreas, and peptidases on the surface of intestinal epithelial cells.
2. Tripeptides, dipeptides, and amino acids are absorbed into intestinal epithelial cells.
3. Amino acids are actively transported into cells under the influence of growth hormone and insulin.
4. Amino acids are used to build new proteins or to serve as a source of energy.

Water and Minerals

Water can move across the intestinal wall in either direction, depending on osmotic conditions. Approximately 99% of the water entering the intestine is absorbed. Most minerals are actively transported across the wall of the small intestine.

REMEMBERING AND UNDERSTANDING

1. What are the functions of the digestive system?
2. What are the major layers, or tunics, of the digestive tract?
3. What are the peritoneum, mesenteries, and retroperitoneal organs?
4. List the functions of the lips, cheeks, and tongue.
5. Distinguish between the deciduous teeth and the permanent teeth. Name the different kinds of teeth.
6. Describe the three parts of a tooth. What are dentin, enamel, and pulp?
7. What is the function of the palate? What are the hard and soft palates?
8. Name and give the locations of the three pairs of salivary glands.
9. What are the functions of saliva?
10. Where is the esophagus located?
11. Describe the three phases of swallowing.
12. Describe the parts of the stomach. How are the muscles in the stomach different from those in the esophagus?
13. What are gastric pits and gastric glands? Name the secretions they produce.
14. List the stomach secretions, and give their functions.
15. Describe the three phases of the regulation of stomach secretion.
16. What are the two kinds of stomach movements? What do they accomplish?
17. Name and describe the three parts of the small intestine.
18. What are circular folds, villi, and microvilli in the small intestine? What are their functions?

19. List the secretions of the small intestine, and give their functions.
20. Describe the kinds of movements in the small intestine, and explain what they accomplish.
21. Describe the anatomy and location of the liver and pancreas, including their duct systems.
22. What are the functions of the liver?
23. Name the exocrine secretions of the pancreas. What are their functions?
24. Describe the parts of the large intestine.
25. How is chyme converted to feces?
26. Describe the defecation reflex.
27. Describe carbohydrate digestion, absorption, and transport.
28. Describe the role of bile salts in lipid digestion and absorption.
29. Describe protein digestion and amino acid absorption. What enzymes are responsible for the digestion?
30. Describe the movement of water into and out of the digestive tract.
31. Describe the effects of aging on the digestive system.

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CRITICAL THINKING

1. While anesthetized, patients sometimes vomit. Given that the anesthetic eliminates the swallowing reflex, explain why it is dangerous for an anesthetized patient to vomit.
2. Achlorhydria (ā-klōr-hī′drē-ă) is a condition in which the stomach stops producing hydrochloric acid and other secretions. What effect does achlorhydria have on the digestive process?

3. Victoria developed a duodenal ulcer during final examination week. Describe the possible reasons. Explain what habits could have contributed to the ulcer, and recommend a reasonable remedy.
4. Many people have a bowel movement shortly after a meal, especially breakfast. Why does this occur?

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER
17

Nutrition, Metabolism, and Body Temperature Regulation

Nutrients include the different substances the body needs to function. Some of these substances must be digested before they are absorbed into the blood, whereas others are absorbed in their original form.

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LEARN TO APPLY IT

Sadie and David loved it when their mothers planned a picnic at the park. They enjoyed running and playing on the jungle gym. Today, Sadie begged her mom to pack a snack of chocolate chip cookies and grape soda. This snack was packed with calories that would give the children lots of energy, but otherwise, it had very little nutritional value. Sadie's mom explained that a snack of fruits, whole-wheat crackers, and water would be much better for everyone.

Describe what the outcome would have been if Sadie's mom allowed them to bring Sadie's suggested snack, which was full of calories, rather than the snack her mother suggested they take to the park.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 12 Digestive System

17.1 NUTRITION

Learning Outcomes *After reading this section, you should be able to*

A. Define nutrition, essential nutrient, and kilocalorie.

B. For carbohydrates, lipids, and proteins, describe their dietary sources, their uses in the body, and the daily recommended amounts of each in the diet.

C. List the common vitamins and minerals, and give a function for each.

When choosing from a menu or selecting food to prepare, we are often more concerned with the food's taste than with its nutritional value. However, knowing about nutrition is important because the food we eat provides us with the energy and the building blocks necessary to synthesize new molecules. What happens if we don't obtain enough vitamins, or if we eat too much sugar and fat? Health claims about foods and food supplements bombard us every day. Which ones are ridiculous, and which ones have merit? A basic understanding of nutrition can help us answer these and other questions so that we can develop a healthful diet. It can also allow us to know which questions currently do not have good answers.

Nutrition (nyu-TRISH-un; to nourish) is the process by which food is taken into and used by the body; it includes digestion, absorption, transport, and metabolism. Nutrition is also the study of food and drink requirements for normal body function.

Nutrients

Nutrients are the chemicals taken into the body that provide energy and building blocks for new molecules. Some substances in food are not nutrients but serve some other role in the body. For example, fiber is not digestible, but it provides bulk to ingested foods and stimulates movement along the digestive tract. Nutrients can be divided into six major classes: (1) carbohydrates, (2) lipids, (3) proteins, (4) vitamins, (5) minerals, and (6) water. Carbohydrates, lipids, and proteins are the major organic nutrients and are broken down by enzymes into their individual subunits during digestion. Subsequently, many of these subunits are broken down further to supply energy, whereas other subunits are used as building blocks for making new carbohydrates, lipids, and proteins. Vitamins, minerals, and water are taken into the

body without being broken down. They are essential participants in the chemical reactions necessary to maintain life. The body requires some nutrients in fairly substantial quantities and others in only minute amounts. Those nutrients needed in only minute amounts are called **trace elements.**

A balanced diet consists of enough nutrients in the correct proportions to support normal body functions. As stated earlier, our nutrients provide energy as well as building blocks for new molecules. **Essential nutrients,** however, are nutrients that must be ingested because the body cannot manufacture them—or it cannot manufacture them in adequate amounts. The essential nutrients include certain amino acids, certain fatty acids, most vitamins, minerals, water, and some carbohydrates. The term *essential* does not mean that the body requires only the essential nutrients. Other nutrients are necessary, but if they are not ingested, the body can synthesize them from the essential nutrients. Most of this synthesis takes place in the liver, which has a remarkable ability to transform and manufacture molecules.

Every 5 years, the U.S. Department of Health and Human Services (HHS) and the U.S. Department of Agriculture (USDA) jointly make recommendations on what Americans should eat to be healthy. The Dietary Guidelines for Americans, 2010, focused on two concepts: (1) balancing calorie intake to obtain and maintain a healthy weight, and (2) increasing consumption of healthy, nutrient-rich foods. In June 2011, the USDA also introduced MyPlate, a food icon to replace the former MyPyramid. MyPlate (figure 17.1) is a simple visual reminder of how to build a healthy meal. The MyPlate icon shows a plate and glass with portions representing foods from the fruits, vegetables, grains, proteins, and dairy food groups. To emphasize the importance of making healthy food choices, half the plate is fruits and vegetables. In addition to the MyPlate icon, the USDA also launched ChooseMyPlate.gov, a website that includes information on how to make healthy dietary choices. The latest recommendations, the Dietary Guidelines for Americans, 2015–2020, focuses on developing healthy eating habits and outlines needed changes in American eating habits to match the recommended dietary habits.

Figure 17.1 **MyPlate**

The MyPlate icon provides a visual reminder for making choices at mealtime, by selecting healthy foods from five food groups. Half the meal should be fruits and vegetables.

US Department of Agriculture

The importance of a healthy diet has been proposed as a key to a healthy life. Two studies completed in 2000 compared the eating habits of 51,529 men and 67,272 women to the government's Healthy Eating Index, a measure of how well a diet conforms to recommended dietary guidelines. Results from these studies demonstrate that eating a healthy diet provides certain health benefits. People who ate the best, according to the index, were compared to those who ate the worst. Men who ate best had a 28% reduction in heart disease and an 11% decrease in chronic diseases compared to men who ate worst. Women who ate best had a 14% reduction in heart disease but no significant decrease in chronic diseases compared to women who ate worst. There was no significant difference in cancer rates between the men and women who ate best compared to those who ate worst.

Kilocalories

The energy the body uses is stored within the chemical bonds of certain nutrients. A **calorie** (KAL-oh-ree; heat) **(cal)** is the amount of energy (heat) necessary to raise the temperature of 1 gram (g) of water 1°C. A **kilocalorie** (KIL-oh-kal-oh-ree) **(kcal)** is 1000 cal and is used to express the larger amounts of energy supplied by foods and released through metabolism. For example, one slice of white bread contains about 75 kcal, 1 cup of whole milk contains 150 kcal, a banana contains 100 kcal, a hot dog contains 170 kcal (not counting the bun and dressings), a McDonald's Big Mac has 540 kcal, and a soft drink adds another 145 kcal. Nutrients provide a predictable amount of energy. For example, each gram of carbohydrate or protein metabolized by the body provides about 4 kcal of energy. Fats contain more energy per unit of weight than carbohydrates and proteins, and they yield about 9 kcal/g.

Table 17.1 lists the kilocalories supplied by some typical foods. A typical diet in the United States consists of 50–60% carbohydrates, 35–45% fats, and 10–15% proteins. Table 17.1 also lists the carbohydrate, fat, and protein composition of some foods.

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TABLE 17.1 Food Composition

Food	Quantity	Food Energy (kcal)	Carbohydrate (g)	Fat (g)	Protein (g)
Dairy Products					
Whole milk (3.3% fat)	1 cup	150	11	8	8
Low-fat milk (2% fat)	1 cup	120	12	5	8
Butter	1 T	100	—	12	—
Grain					
Bread, white enriched	1 slice	75	24	1	2
Bread, whole-wheat	1 slice	65	14	1	3
Fruit					
Apple	1	80	20	1	—
Banana	1	100	25	—	1
Orange	1	65	16	—	1
Vegetables					
Corn, canned	1 cup	140	33	1	4
Peas, canned	1 cup	150	29	1	8
Lettuce	1 cup	5	2	—	—
Celery	1 cup	20	5	—	1
Potato, baked	1 large	145	33	—	4
Meat, Fish, and Poultry					
Lean ground beef (10% fat)	3 oz	185	—	10	23
Shrimp, french fried	3 oz	190	9	9	17
Tuna, canned	3 oz	170	—	7	24
Chicken breast, fried	3 oz	160	1	5	26
Bacon	2 slices	85	—	8	4
Hot dog	1	170	1	15	7
Fast Foods					
McDonald's Egg McMuffin	1	300	30	12	18
McDonald's Big Mac	1	540	45	29	25
Taco Bell Beef Burrito Supreme	1	420	53	15	17
Arby's roast beef, regular	1	360	37	14	22
Pizza Hut Super Supreme	1 slice	245	29	17	14

Food	Quantity	Food Energy (kcal)	Carbohydrate (g)	Fat (g)	Protein (g)
Long John Silver's fish	2 pieces	520	32	34	24
Dairy Queen Oreo Cookie Blizzard, medium	1	680	100	25	14
Desserts					
Chocolate chip cookie	1	50	7	2	1
Apple pie	1 piece	135	49	14	3
Soft ice cream	1 cup	377	38	23	7
Beverage					
Cola soft drink	12 oz	145	37	—	—
Beer	12 oz	144	13	—	—
Wine	$3\frac{1}{2}$ oz	73	2	—	—
Hard liquor (86 proof)	$1\frac{1}{2}$ oz	105	—	—	—
Miscellaneous					
Egg	1	80	1	6	6
Mayonnaise	1 T	100	—	11	—
Sugar	1 T	45	12	—	—

A kilocalorie is often called a *Calorie* (with a capital *C*). Unfortunately, this usage has resulted in confusion of the term *calorie* (with a lowercase *c*) with *Calorie* (with a capital *C*). It is common practice on food labels to use the term *calorie* when *Calorie* (*kilocalorie*) is the proper term.

Carbohydrates

Sources in the Diet

Carbohydrates (kar-boh-HIGH-drates) include monosaccharides, disaccharides, and polysaccharides (see chapter 2). The most common monosaccharides in the diet are glucose and fructose. Plants capture energy from sunlight and use that energy to produce glucose, which can be found in vegetables, fruits, molasses, honey, and syrup. Fructose is most often derived from fruits and berries. Although most of the carbohydrates we ingest are derived from plants, lactose is an example of a sugar derived from animals.

The disaccharide sucrose (table sugar) is what most people think of when they use the term *sugar*. Sucrose consists of one glucose and one fructose molecule joined together. The principal sources for sucrose are sugarcane and sugar beets. Maltose (malt sugar) is a disaccharide derived from germinating cereals. It is a combination of two glucose molecules. Lactose (milk sugar) consists of one glucose molecule and one galactose molecule.

Complex carbohydrates are large polysaccharides, which are composed of long chains of glucose (see figure 2.12). Examples of complex carbohydrates include

starch, glycogen, and cellulose. Though all of these are composed of long chains of glucose, they differ from one another in the arrangement of the glucose molecules and the structure of the chemical bonds holding them together.

Starch is an energy-storage molecule in plants and is found primarily in vegetables, fruits, and grains. Glycogen is an energy-storage molecule in animals and is located primarily in muscle and in the liver. Cellulose forms plant cell walls.

Uses of Carbohydrates in the Body

During digestion, polysaccharides and disaccharides are split into monosaccharides, which are absorbed into the blood (see chapter 16). Humans have enzymes that can break the bonds between the glucose molecules of starch and glycogen, but they do not have the enzymes necessary to digest cellulose, the polysaccharide of plant cell walls. Therefore, it is important to thoroughly cook or chew plant matter. Cooking and chewing break down the plant cell walls and expose the starches contained inside the cells to digestive enzymes. The undigested cellulose provides fiber, or "roughage," which increases the bulk of feces, making it easier to defecate.

The liver has the ability to chemically alter many of the absorbed nutrients, providing the cells of the body with the molecules they need in order to function normally. Fructose and other monosaccharides absorbed into the blood are converted into glucose by the liver. Glucose, whether absorbed directly from the digestive tract or synthesized by the liver, is an energy source used to produce ATP. Because the brain relies almost entirely on glucose for its energy, the body carefully regulates blood glucose levels.

If an excess amount of glucose is present in the diet, the glucose is used to make glycogen, which is stored in muscle and in the liver. Glycogen can be rapidly converted back to glucose when energy is needed. Because cells can store only a limited amount of glycogen, additional glucose that is ingested is converted into lipids for long-term storage in adipose tissue.

In addition to being used as an energy source, sugars form part of deoxyribonucleic acid (DNA), ribonucleic acid (RNA), and ATP molecules. Sugars also combine with proteins to form glycoproteins, some of which function as receptor molecules on the outer surface of the cell membrane.

Recommended Consumption of Carbohydrates

According to the Dietary Guidelines Advisory Committee, the **Acceptable Macronutrient Distribution Range (AMDR)** for carbohydrates is 45–65% of total kilocalories. Although a minimum level of carbohydrates is not known, it is assumed that amounts of 100 g or less per day result in overuse of the body's proteins and lipids for energy sources. Because muscles are primarily protein, the use of proteins for energy can result in the breakdown of muscle tissue. The extensive use of lipids as an energy source can result in acidosis (see chapter 18).

Complex carbohydrates are recommended in the diet because many starchy foods contain other valuable nutrients, such as vitamins and minerals. In addition, the

slower rate of digestion and absorption of complex carbohydrates does not result in large increases and decreases in blood glucose level, as the consumption of large amounts of simple sugars does. Eating whole grains also helps a person meet the recommended fiber intake (25 g/day for females and 38 g/day for males). Foods containing large amounts of simple sugars, such as soft drinks and candy, are rich in carbohydrates but have few other nutrients. For example, a typical soft drink is mostly sucrose, containing 9 teaspoons of sugar per 12-oz container. In excess, the consumption of these kinds of foods usually results in obesity and tooth decay. (This information may be useful for answering the Learn to Apply It question at the beginning of the chapter.)

Lipids

Sources in the Diet

Lipids (LIP-ids) include triglycerides, steroids, phospholipids, and fat-soluble vitamins. **Triglycerides** (trie-GLISS-eh-rides), also called *triacylglycerols* (try-AS-il-GLISS-er-ols), are the most common type of lipid in the diet, accounting for about 95% of the total lipid intake. Triglyceride molecules consist of three fatty acids bound to one glycerol molecule (see figure 2.13). Triglycerides are often referred to as fats. If the fat is a liquid at room temperature, it is referred to as an oil. Fats are **saturated** if their fatty acids have only single covalent bonds between carbon atoms and **unsaturated** if they have one or more double bonds (see figure 2.14). **Monounsaturated fats** have one double bond, and **polyunsaturated fats** have two or more double bonds. Saturated fats are found in meat, dairy products, eggs, nuts, coconut oil, and palm oil (table 17.1). Monounsaturated fats include olive and peanut oils; polyunsaturated fats are found in fish, safflower, sunflower, and corn oils.

Solid fats, mainly shortening and margarine, work better than liquid oils in preparing some foods, such as pastries. Polyunsaturated vegetable oils can be changed from a liquid to a solid by making them more saturated—that is, by decreasing the number of double covalent bonds in their polyunsaturated fatty acids. To saturate an unsaturated oil, the oil can be *hydrogenated,* which means that hydrogen gas is bubbled through the oil, producing a change in molecular shape that solidifies the oil. The more saturated the product, the harder it becomes at room temperature. These processed fats are usually referred to as ***trans* fats.**

Processed foods and oils account for most of the *trans* fats in the American diet, although some *trans* fats occur naturally in food from animal sources. *Trans* fatty acids raise the concentration of low-density lipoproteins and lower the concentration of high-density lipoproteins in the blood (see chapter 16). These changes are associated with a greater risk of cardiovascular disease. The Food and Drug Administration (FDA) requires that food labels include a detailed list of the amounts of saturated and *trans* fats, allowing the consumer to make better dietary choices.

The remaining 5% of ingested lipids include steroids and phospholipids. **Cholesterol** (koh-LES-ter-ol) is a steroid (see chapter 2) found in high concentrations in the brain, the liver, and egg yolks, but it is also present in whole

milk, cheese, butter, and meats. Cholesterol is not found in plants. Phospholipids, such as **lecithin** (LES-ih-thin; *lekithos,* egg yolk), are major components of cell membranes and are found in a variety of foods. A good source of lecithin is egg yolks.

Uses of Lipids in the Body

Triglycerides are an important source of energy that can be used to produce ATP. A gram of triglyceride delivers over twice as many calories as does a gram of carbohydrate or protein. Some cells, such as skeletal muscle cells, derive most of their energy from triglycerides.

Ingested triglyceride molecules not immediately used are stored in adipose tissue or in the liver. When energy is required, the stored triglycerides are broken down, and the fatty acids are released into the blood. The fatty acids can be taken up and used by various tissues. In addition to storing energy, adipose tissue surrounds, pads, and protects organs. Adipose tissue located under the skin is an insulator, which helps reduce heat loss.

Cholesterol is an important molecule that is obtained in food, or it can be manufactured by the liver and most other tissues. Cholesterol has many functions in the body. It is a component of the cell membrane. Cholesterol can be modified to form other useful molecules, such as bile salts and steroid hormones. Bile salts emulsify ingested fats, which is important for fat digestion and absorption in the small intestine (see chapter 16). Steroid hormones include the sex hormones estrogen, progesterone, and testosterone, which regulate the reproductive system.

Other important lipids in the body include phospholipids, lecithin, and eicosanoids. Phospholipids (see chapter 2) are part of the cell membrane and are used to construct myelin sheaths around the axons of nerve cells. Lecithin is found in bile and helps emulsify fats. Eicosanoids, which are derived from fatty acids, are involved in inflammation, tissue repair, smooth muscle contraction, and other functions.

Recommended Consumption of Lipids

The AMDR for fats is 20–35% for adults, 25–35% for children and adolescents 4 to 18 years of age, and 30–35% for children 2 to 3 years of age. Saturated fats should be no more than 10% of total kilocalories, or as low as possible. Most dietary fat should come from sources of polyunsaturated and monounsaturated fats. Cholesterol should be limited to 300 mg (the amount in one egg yolk) or less per day, and *trans* fat consumption should be as low as possible. These guidelines reflect the belief that excess amounts of fats, especially saturated fats, *trans* fats, and cholesterol, contribute to cardiovascular disease. The typical American diet derives 35–45% of its kilocalories from fats, indicating that most Americans need to reduce their fat consumption. See table 17.1 for a sampling of the fat composition in foods.

CLINICAL IMPACT

Free Radicals and Antioxidants

Free radicals are molecules that are missing an electron and are produced by the body as part of normal metabolism. Free radicals can replace the missing electron by taking an electron from cell molecules, such as lipids, proteins, or DNA, resulting in damage to the cell. Damage from free radicals may contribute to aging and certain diseases, such as atherosclerosis and cancer.

The loss of an electron from a molecule is called oxidation. **Antioxidants** are substances that prevent oxidation of cell components by donating an electron to free radicals. Examples of antioxidants are beta carotene (provitamin A), vitamin C, and vitamin E.

Many studies have attempted to determine whether taking large doses of antioxidants is beneficial. Among scientists establishing the RDAs, the best evidence presently available does not support the claim that large doses of antioxidants can prevent chronic disease or otherwise improve health. On the other hand, the amount of antioxidants normally found in a balanced diet (including fruits and vegetables rich in antioxidants), combined with the complex mix of other chemicals found in food, can be beneficial.

If a person does not consume enough fats, the body can synthesize fats from carbohydrates and proteins. **Linoleic** (lin-oh-LEE-ik; *linum,* flax + *oleum,* oil) **acid** and **alpha-linolenic acid** are called **essential fatty acids** because the body cannot synthesize them, so they must be ingested. They are found in plant oils, such as canola or soybean oil.

The essential fatty acids are used to synthesize molecules that affect blood clotting. Linoleic acid can be converted to **arachidonic** (ah-rak-ih-DON-ik; *arakis*) **acid,** which is used to produce prostaglandins that *increase* blood clotting. Alpha-linolenic acid can be converted to **eicosapentaenoic** (eye-koh-sah-pen-tah-NO-ik) **acid (ePa),** which is used to produce prostaglandins that *decrease* blood clotting. Normally, most prostaglandins are synthesized from linoleic acid because it is more plentiful in the diet. However, individuals who consume foods rich in EPA, such as herring, salmon, tuna, and sardines, increase the synthesis of prostaglandins from EPA. People who eat these fish two or more times per week have a lower risk of heart attack than those who don't, probably because of reduced chance of abnormal blood clotting. For those who cannot or choose not to eat the recommended number of servings of fish, fish oil supplements are an alternative.

Proteins

Sources in the Diet

Proteins (PRO-teens) are chains of amino acids (see figure 2.17). They are found in most of the plant and animal products we eat (see table 17.1). Proteins in the body are constructed of 20 different kinds of amino acids, which are divided into two groups:

(1) essential amino acids and (2) nonessential amino acids. The body cannot synthesize **essential amino acids,** so they must be obtained in the diet. There are nine essential amino acids: (1) histidine, (2) isoleucine, (3) leucine, (4) lysine, (5) methionine, (6) phenylalanine, (7) threonine, (8) tryptophan, and (9) valine. **Nonessential amino acids** are necessary to construct our proteins but do not necessarily need to be ingested because they can be synthesized from the essential amino acids. A food that is considered a **complete protein** contains all nine essential amino acids in the needed proportions, whereas a food designated an incomplete protein does not. Animal proteins tend to be complete proteins, whereas plant proteins tend to be incomplete. However, some plant-based foods, such as soy and quinoa, are sources of complete proteins. Examples of animal complete proteins are red meat, fish, poultry, milk, cheese, and eggs. Examples of incomplete proteins are leafy green vegetables, grains, and legumes (peas and beans). If two incomplete proteins, such as rice and beans, are ingested, each can provide amino acids lacking in the other. Thus, vegetarian or vegan diets, if balanced correctly, provide all the essential amino acids.

Uses of Proteins in the Body

Proteins perform numerous functions in the human body, as the following examples illustrate. Collagen provides structural strength in connective tissue, as does keratin in the skin. The combination of actin and myosin makes muscle contraction possible. Enzymes are responsible for regulating the rate of chemical reactions in the body, and protein hormones regulate many physiological processes (see chapter 10). Proteins in the blood act as clotting factors, transport molecules, and buffers (which limit changes in pH). Proteins also function as ion channels, carrier molecules, and receptor molecules in the cell membrane. Antibodies, lymphokines, and complement are all proteins that function in the immune system.

Proteins can also be used as a source of energy, yielding approximately the same amount of energy as that derived from carbohydrates. If excess proteins are ingested, the body can use the energy from the proteins to produce glycogen and lipid molecules, which can be stored. When protein intake is adequate in a healthy adult, the synthesis and breakdown of proteins occur at the same rate.

Recommended Consumption of Proteins

The AMDR for protein is 10–35% of total kilocalories. See table 17.1 for a sampling of the protein composition in foods.

Vitamins

Vitamins (VIE-tah-mins; life-giving chemicals) are organic molecules that exist in minute quantities in food and are essential to normal metabolism (table 17.2). **Essential vitamins** cannot be produced by the body and must be obtained through the diet. Because no single food item or nutrient class provides all the essential vitamins, it is necessary to maintain a balanced diet by eating a variety of foods. The absence of an essential vitamin in the diet can result in a specific deficiency disease.

A few vitamins, such as vitamin K, are produced by intestinal bacteria, and a few others can be formed by the body from substances called provitamins. A **provitamin** is a part of a vitamin that the body can assemble or modify into a functional vitamin. Beta carotene is an example of a provitamin that can be modified by the body to form vitamin A. The other provitamins are **7-dehydrocholesterol** (dee-HIGH-droh-koh-LES-ter-ol), which can be converted to vitamin D, and **tryptophan** (TRIP-toh-fan), which can be converted to niacin.

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TABLE 17.2 The Principal Vitamins

Vitamin	Fat- (F) or Water- (W) Soluble	Source	Function	Symptoms of Deficiency	Reference Daily Intake (RDI)s[a]
A (retinol)	F	From provitamin carotene found in yellow and green vegetables; preformed in liver, egg yolk, butter, and milk	Necessary for rhodopsin synthesis, normal health of epithelial cells, and bone and tooth growth	Rhodopsin deficiency, night blindness, delayed growth, skin disorders, and increased infection risk	900 RE[b]
B_1 (thiamine)	W	Yeast, grains, and milk	Involved in carbohydrate and amino acid metabolism; necessary for growth	Beriberi—muscle weakness (including cardiac muscle), neuritis, and paralysis	1.2 mg
B_2 (riboflavin)	W	Green vegetables, liver, wheat germ, milk, and eggs	Component of flavin adenine dinucleotide; involved in citric acid cycle	Eye disorders and skin cracking, especially at corners of the mouth	1.3 mg
B_3 (niacin)	W	Fish, liver, red meat, yeast, grains, peas, beans, and nuts	Component of nicotinamide adenine dinucleotide; involved in glycolysis and citric acid cycle	Pellagra—diarrhea, dermatitis, and nervous system disorder	16 mg

Vitamin	Fat- (F) or Water- (W) Soluble	Source	Function	Symptoms of Deficiency	Reference Daily Intake (RDI)s[a]
Pantothenic acid	W	Liver, yeast, green vegetables, grains, and intestinal bacteria	Constituent of coenzyme-A; glucose production from lipids and amino acids; steroid hormone synthesis	Neuromuscular dysfunction and fatigue	5 mg
Biotin	W	Liver, yeast, eggs, and intestinal bacteria	Fatty acid and nucleic acid synthesis; movement of pyruvic acid into citric acid cycle	Mental and muscle dysfunction, fatigue, and nausea	30 μg
B_6 (pyridoxine)	W	Fish, liver, yeast, tomatoes, and intestinal bacteria	Involved in amino acid metabolism	Dermatitis, delayed growth, and nausea	1.7 mg
Folate	W	Liver, green leafy vegetables, and intestinal bacteria	Nucleic acid synthesis; hematopoiesis; prevents birth defects	Macrocytic anemia (enlarged red blood cells) and spina bifida	0.4 mg
B_{12} (cobalamins)	W	Liver, red meat, milk, and eggs	Necessary for red blood cell production, some nucleic acid and amino acid metabolism	Pernicious anemia and nervous system disorders	2.4 μg
C (ascorbic acid)	W	Citrus fruit, tomatoes, and green vegetables	Collagen synthesis; general protein metabolism	Scurvy—defective bone formation and poor wound healing	90 mg
D (cholecalciferol, ergosterol)	F	Fish liver oil, enriched milk, and eggs; provitamin D converted by sunlight to cholecalciferol in the skin	Promotes calcium and phosphorus use; normal growth and bone and tooth formation	Rickets—poorly developed, weak bones, osteomalacia; bone reabsorption	10 μg[c]

Vitamin	Fat-(F) or Water-(W) Soluble	Source	Function	Symptoms of Deficiency	Reference Daily Intake (RDI)s[a]
E (tocopherol, tocotrienols)	F	Wheat germ; cottonseed, palm, and rice oils; grain; liver; and lettuce	Prevents oxidation of cell membranes and DNA	Hemolysis of red blood cells	15 mg
K (phylloquinone)	F	Alfalfa, liver, spinach, vegetable oils, cabbage, and intestinal bacteria	Required for synthesis of a number of clotting factors	Excessive bleeding due to impaired blood clotting	120 µg

[a] RDIs for people over 4 years of age; IU = international units.
[b] Retinol equivalents (RE). 1 retinol equivalent = 1 ìg retinol or 6 ìg â-carotene.
[c] As cholecalciferol. 1 ìg cholecalciferol = 40 IU (international units) vitamin D.

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Vitamins are not broken down by catabolism but are used by the body in their original or slightly modified forms. After the chemical structure of a vitamin is destroyed, its function is lost. The chemical structure of many vitamins is destroyed by heat, as when food is overcooked.

Most vitamins function as **coenzymes,** which combine with enzymes to make the enzymes functional (see chapter 2). Table 17.2 summarizes the function and sources of the vitamins, and briefly describes symptoms of deficiencies.

Apply It 1

Explain what would happen if vitamins were broken down during the process of digestion rather than being absorbed intact into the circulation.

Vitamins are either fat-soluble or water-soluble. **Fat-soluble vitamins,** such as vitamins A, D, E, and K, are absorbed from the intestine along with lipids. Some of them can be stored in the body for a long time. Because they can be stored, these vitamins can accumulate in the body to the point of toxicity. **Water-soluble vitamins,** such as the B vitamins and vitamin C, are absorbed with water from the intestinal tract and typically remain in the body only a short time before being excreted in the urine.

Vitamins were first identified at the beginning of the twentieth century. They were found to be associated with certain foods that were known to protect people from diseases such as rickets and beriberi. In 1941, the first Food and Nutrition Board established the **Recommended Dietary Allowances (RDAs),** which are the

nutrient intakes that are sufficient to meet the needs of nearly all people in certain age and gender groups. RDAs were established for different-aged males and females, starting with infants and continuing on to adults. RDAs were also set for pregnant and lactating females. The RDAs have been reevaluated every 4–5 years and updated, when necessary, on the basis of new information.

The RDAs establish a minimum intake of vitamins and minerals that should protect almost everyone (97%) in a given group from diseases caused by vitamin or mineral deficiencies. Although personal requirements can vary, the RDAs are a good benchmark. The farther below the RDAs an individual's dietary intake is, the more likely that person is to develop a nutritional deficiency. On the other hand, consuming too much of some nutrients can have harmful effects. For example, the long-term ingestion of 3–10 times the RDA for vitamin A can cause bone and muscle pain, skin disorders, hair loss, and an enlarged liver. Consuming 5–10 times the RDA of vitamin D over the long term can result in calcium deposits in the kidneys, heart, and blood vessels, and regularly consuming more than 2 g (which is more than 20 times the RDA) of vitamin C daily can cause stomach inflammation and diarrhea.

Minerals

Minerals (MIN-er-als) are inorganic nutrients that are essential for normal metabolic functions. People ingest minerals alone or in combination with organic molecules. They constitute about 4–5% of total body weight and are involved in a number of important functions, such as establishing resting membrane potentials and generating action potentials; adding mechanical strength to bones and teeth; combining with organic molecules; and acting as coenzymes, buffers, or regulators of osmotic pressure. A balanced diet can provide all the necessary minerals, with a few possible exceptions. For example, individuals suffering from chronic bleeding, including females who experience excessive menstrual bleeding, may need an iron supplement. Table 17.3 lists some minerals and their functions.

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TABLE 17.3 Important Minerals

Mineral	Function	Symptoms of Deficiency	Reference Daily Intake (RDI)s[a]
Calcium	Bone and teeth formation; blood clotting; muscle activity; and nerve function	Spontaneous action potential generation in neurons and tetanic muscle contractions	1300 mg
Chlorine	Blood acid-base balance; hydrochloric acid production in stomach	Acid-base imbalance	2.3 g[b]
Chromium	Associated with enzymes in glucose metabolism	Unknown	35 μg

Mineral	Function	Symptoms of Deficiency	Reference Daily Intake (RDI)s[a]
Cobalt	Component of vitamin B_{12}; red blood cell production	Anemia	Unknown
Copper	Hemoglobin and melanin production; electron- transport system	Anemia and loss of energy	0.9 mg
Fluorine	Provides extra strength in teeth; prevents dental caries	No real pathology	4 mg
Iodine	Thyroid hormone production; maintenance of normal metabolic rate	Goiter and decrease in normal metabolism	150 μg
Iron	Component of hemoglobin; ATP production in electron-transport system	Anemia, decreased O_2 transport, and energy loss	18 mg
Magnesium	Coenzyme constituent; bone formation; muscle and nerve function	Increased nervous system irritability, vasodilation, and arrhythmias	420 mg
Manganese	Hemoglobin synthesis; growth; activation of several enzymes	Tremors and convulsions	2.3 mg
Molybdenum	Enzyme component	Unknown	45 μg
Phosphorus	Bone and teeth formation; important in energy transfer (ATP); component of nucleic acids	Loss of energy and cellular function	1250 mg
Potassium	Muscle and nerve function	Muscle weakness, abnormal electrocardiogram, and alkaline urine	4.7 g
Selenium	Component of many enzymes	Unknown	55 μg
Sodium	Osmotic pressure regulation; nerve and muscle function	Nausea, vomiting, exhaustion, and dizziness	1.5 g[b]
Sulfur	Component of hormones, several vitamins, and proteins	Unknown	Unknown
Zinc	Component of several enzymes; carbon dioxide transport and metabolism; necessary for protein metabolism	Deficient CO_2 transport and deficient protein metabolism	11 mg

[a] RDIs for people over 4 years of age, except for sodium.
[b] 3.8 g sodium chloride (table salt)

Daily Values

Daily Values appear on food labels to help consumers plan a healthful diet and to minimize confusion (figure 17.2). However, not all possible Daily Values are required

to be listed on food labels. Daily Values are based on two other sets of reference values—(1) Reference Daily Intakes and (2) Daily Reference Values:

- **Reference Daily Intakes (RDIs)** are based on the 1968 RDAs for certain vitamins and minerals. RDIs have been set for four categories of people: infants, toddlers, people over 4 years of age, and pregnant or lactating females. Generally, the RDIs are set to the highest 1968 RDA value of an age category. For example, the highest RDA for iron in males over 4 years of age is 10 mg/day and for females over 4 years of age is 18 mg/day. Thus, the RDI for iron is set at 18 mg/day.
- **Daily Reference Values (DRVs)** are set for total fat, saturated fat, cholesterol, total carbohydrate, dietary fiber, sodium, potassium, and protein.

Nutrition Facts

4 servings per container
Serving size **1 cup (227g)**

Amount per serving
Calories **280**

	% Daily Value*
Total Fat 9g	**12%**
Saturated Fat 4.5g	**23%**
Trans Fat 0g	
Cholesterol 35mg	**12%**
Sodium 850mg	**37%**
Total Carbohydrate 34g	**12%**
Dietary Fiber 4g	**14%**
Total Sugars 6g	
Includes 0g Added Sugars	**0%**
Protein 15g	
Vitamin D 0mcg	0%
Calcium 320mg	25%
Iron 1.6mg	8%
Potassium 510mg	10%

* The % Daily Value (DV) tells you how much a nutrient in a serving of food contributes to a daily diet. 2,000 calories a day is used for general nutrition advice.

Figure 17.2 **Current Food Label, Adopted in 2016**
The current food label highlights calorie counts and serving size more prominently than the older food label.
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The Daily Values appearing on food labels are based on a 2000-kcal reference diet, which approximates the weight maintenance requirements of (1) postmenopausal females, (2) adult females who exercise moderately, (3) adolescent females, and (4) sedentary males (figure 17.2). On large food labels, additional information is listed based on a daily intake of 2500 kcal, which is adequate for young men.

The Daily Values for energy-producing nutrients are determined as a percentage of daily kilocaloric intake:

- 60% for carbohydrates
- 30% for total fats
- 10% for saturated fats
- 10% for proteins

The Daily Value for fiber is 14 g for each 1000 kcal of intake. The Daily Values for a nutrient in a 2000 kcal/day diet can be calculated on the basis of the recommended daily percentage of the nutrient and the kilocalories in a gram of the nutrient. For example, carbohydrates should constitute 60% of a 2000 kcal/day diet, or 1200 kcal/day (0.60 × 2000). Because there are 4 kilocalories in a gram of carbohydrate, the Daily Value for carbohydrate is 300 g/day (1200/4).

The Daily Values for some nutrients are the uppermost limit considered desirable because of the link between these nutrients and certain diseases. Thus, the Daily Values for total fats are less than 65 g; saturated fats, less than 20 g; and cholesterol, less than 300 mg because of their association with increased risk of heart disease. The Daily Value for sodium is less than 2400 mg because of its association with high blood pressure in some people.

For a particular food, the Daily Values are used to calculate the **Percent Daily Value (% Daily Value)** for some of the nutrients in one serving of the food (figure 17.2). For example, if a serving of food has 3 g of fat and the Daily Value for total fat is 65 g, then the % Daily Value is 5% (3/65 = 0.05, or 5%). The Food and Drug Administration (FDA) requires % Daily Values to be on food labels, so that the public has useful and accurate dietary information.

In 2016, the FDA approved a major revision of food nutrition labels. The new nutrition labels display calorie counts more prominently and represent more reasonable serving sizes (figure 17.2). Manufacturers are required to list the actual amounts of vitamin D, calcium, iron, and potassium; however, listing the amounts of other vitamins is optional. Manufacturers are also required to list the amount of added sugar on the nutrition label, to assist the consumer in making better choices about total sugar intake, which has been linked to the current increase in obesity in the United States. Saturated fat and *trans* fat information is also included, but the "Calories from Fat" on the old label is no longer included. This reflects the modern view of nutritionists that the types of fats we ingest are more important than the amount. A footnote that better explains the Daily Values and calories has also been added to the new label.

Apply It 2

One serving of a food has 30 g of carbohydrate. What % Daily Value for carbohydrate is on the food label for this food?

The % Daily Values for nutrients related to energy consumption are based on a 2000 kcal/day diet. For individuals who maintain their weight on a 2000 kcal/day diet, the total of the % Daily Values for each of these nutrients should be no more than 100%. However, for individuals consuming more or fewer than 2000 kcal per

day, the total of the % Daily Values can be more or fewer than 100%. For example, for a person consuming 2200 kcal/day, the total of the % Daily Values for each of these nutrients should be no more than 110% because 2200/2000 = 1.10, or 110%.

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Apply It 3

Suppose a person consumes 1800 kcal/day. What total % Daily Values for energy-producing nutrients is recommended?

When using the % Daily Values of a food to determine how the amounts of certain nutrients in the food fit into the overall diet, the number of servings in a container or package needs to be considered. For example, suppose a small (2.25-oz) bag of corn chips has a % Daily Value of 16% for total fat. A person might suppose that eating the bag of chips accounts for 16% of total fat for the day. The bag, however, contains 2.5 servings. All the chips in the bag account for 40% (16% × 2.5) of the maximum recommended total fat.

17.2 METABOLISM

Learning Outcomes *After reading this section, you should be able to*

A. Define metabolism, anabolism, and catabolism.
B. List three ways in which enzyme activity is controlled.
C. Describe glycolysis and name its products.
D. Describe the citric acid cycle and name its products.
E. Describe the electron-transport chain and how ATP is produced in the process.
F. Explain how the breakdown of glucose yields 2 ATP molecules in anaerobic respiration and 32 ATP molecules in aerobic respiration.
G. Describe the basic steps involved in using lipids and amino acids as energy sources.
H. Differentiate between the absorptive and postabsorptive metabolic states.
I. Define metabolic rate.

Metabolism (meh-TAB-oh-lizm; change) is the total of all the chemical reactions that occur in the body. It consists of **catabolism** (kah-TAB-oh-lizm), the energy-releasing process by which large molecules are broken down into smaller ones, and **anabolism** (an-AB-oh-lizm), the energy-requiring process by which small molecules are joined to form larger ones. Catabolism begins during the process of digestion and is concluded within individual cells. Anabolism occurs in all cells of the body as they divide to form new cells, maintain their own intracellular structure, and produce molecules such as hormones, neurotransmitters, or extracellular matrix molecules for export. The energy derived from catabolism is used to drive anabolic reactions.

Metabolism can be divided into the chemical reactions that occur during digestion in the digestive tract and the chemical reactions that occur in the cells of the body after the products of digestion are taken up by cells. The chemical reactions that

occur within cells are often referred to as **cellular metabolism.** Figure 17.3 illustrates the connections between the major classes of reactions that occur in cells.

❶ The digestive products of carbohydrates, proteins, and lipids are absorbed from the small intestine and move into the blood. These nutrients are then delivered to cells, where they can be further broken down through catabolism. The energy released during this breakdown can be used to combine **ADP** and an inorganic phosphate group (P_i) to form **ATP.**

❷ ATP is often called the energy currency of the cell. When ATP is broken down to ADP, cells can use the released energy for active transport, muscle contraction, and anabolic reactions, such as protein synthesis. Because the body has high energy demands, it uses ATP rapidly.

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PROCESS Figure

PROCESS Figure 17.3 APR **ATP Derived from Catabolic Reactions Drives Anabolic Reactions**

Cells use energy derived from catabolic reactions to power anabolic reactions.

Understand **Considering the information provided in table 3.1, identify a cellular organelle involved in an anabolic reaction.**

When discussing the production of ATP, most often we focus on the breakdown of carbohydrates. Though carbohydrates are the cell's most readily available energy source, lipids and proteins can also be metabolized to produce ATP. Figure 17.4 presents an overview of the metabolism of all three of these nutrients. Each of these will be discussed in more detail later in this section.

❶ Carbohydrates are digested to monosaccharides, such as glucose. Cells can further break down the monosaccharides to produce ATP. Each step of this process—glycolysis, the citric acid cycle, and the electron-transport chain—is described below.

❷ Lipids, such as triglycerides, are broken down into fatty acids and glycerol, which then can enter a metabolic pathway similar to the pathway by which carbohydrates generate ATP.

❸ Proteins are digested into amino acids. Amino acids either enter the metabolic pathway that resembles carbohydrate breakdown or are broken down further. The breakdown products can then enter the metabolic pathways to generate ATP.

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PROCESS Figure

PROCESS Figure 17.4 APR **Overall Pathways for the Metabolism of Food**

Carbohydrates, lipids, and proteins enter biochemical pathways to produce energy in the cell.

Shutterstock/Anna Kucher

Apply **If a toxin blocked the process of glycolysis, which nutrients, and specifically which components, might still be metabolized for ATP production?**

Regulation of Metabolism

The products of digestion, such as glucose, fatty acids, and amino acids, are molecules containing energy within their chemical bonds. A series of chemical reactions, called a **biochemical pathway,** controls the energy release from these molecules. At some of the steps, small amounts of energy are released; some of this energy is used to synthesize ATP (figure 17.5). About 40% of the energy in foods is incorporated into ATP; the rest is lost as heat.

Figure 17.5 **Biochemical Pathway**
Each step in the pathway is regulated by a specific enzyme. Substance D can inhibit enzyme 1, thus regulating its own production. Some of the energy released by reactions in the pathway can be used to synthesize ATP.

There are several different biochemical pathways inside cells. Each step of these biochemical pathways involves a specific enzyme. As a consequence, which pathways function and how much each pathway is used are determined by these enzymes (see chapter 2). In turn, enzymes are regulated in several ways:

1. *Enzyme synthesis*. Enzymes are proteins, and their synthesis depends on DNA (see chapter 3). Thus, the types and amounts of enzymes present in cells are under genetic control.
2. *Receptor-mediated enzyme activity*. The combination of a chemical signal, such as a neurotransmitter or hormone, with a membrane-bound or intracellular receptor can activate or inhibit enzyme activity (see chapter 10).
3. *Product control of enzyme activity*. The end product of a biochemical pathway can inhibit the enzyme responsible for the first reaction in the pathway. This negative-feedback regulation prevents accumulation of the intermediate products and the end product of the pathway (figure 17.5).

Many metabolic disorders result from missing or dysfunctional enzymes. For example, in **Tay-Sachs disease,** the breakdown of lipids within lysosomes is impaired. Thus, the intermediate products of lipid metabolism accumulate abnormally, resulting in the destruction of neurons and death of the individual by age 3–4 years. **Phenylketonuria** (FEN-il-kee-toh-NOO-ree-a) (**PKU**) results from the inability to convert the amino acid phenylalanine to tyrosine. Therefore, phenylalanine accumulates in nerve cells and causes brain damage. Unlike Tay-Sachs

disease, the extent of damage resulting from PKU can be limited by controlling the diet. Restricting the intake of phenylalanine is an effective treatment for PKU because it reduces the accumulation of phenylalanine in the body. This subsequently reduces the amount of damage to the brain.

Carbohydrate Metabolism

Monosaccharides are the breakdown products of carbohydrate digestion. Of these, glucose is the most important monosaccharide in terms of cellular metabolism. Glucose is transported in the blood to all tissues of the body, where it is used as a source of energy. Any excess glucose in the blood following a meal can be used to form **glycogen** (GLIE-koh-jen; *glyks,* sweet), or it can be partially broken down and the components used to form lipids. Glycogen is a short-term energy-storage molecule and the body can store it in limited amounts, whereas lipids are long-term, energy-storage molecules that the body can store in large amounts. Most of the body's glycogen is in skeletal muscle and in the liver.

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Glycolysis

Glycolysis (glye-KOHL-ih-sis) is a series of chemical reactions that occurs in the fluid part of cytoplasm surrounding the organelles. It results in the breakdown of glucose to two **pyruvic** (pye-ROO-vik) **acid** molecules (figure 17.6). When glucose is converted to pyruvic acid, two ATP molecules are used and four ATP molecules are produced, for a net gain of two ATP molecules.

PROCESS Figure

PROCESS Figure 17.6 **Glycolysis and Anaerobic Respiration**
Anaerobic respiration occurs in the absence of O_2, when glucose is broken down to produce lactic acid and ATP.

Understand **How many carbon atoms does a lactate molecule contain? Explain your answer.**

Glucose consists of 6 carbon atoms, 12 hydrogen atoms, and 6 oxygen atoms covalently bonded together. During the breakdown of glucose, a hydrogen ion (H^+) and two electrons (e^-) are released and can attach to a **carrier molecule,** which moves the H^+ and electrons to other parts of the cell. A very common carrier molecule in cells is **nicotinamide adenine dinucleotide** (nik-oh-TIN-a-myde AD-eh-neen dye-NOO-klee-oh-tide) **(NADH):**

$$NAD^+ + 2\,e^- + H^+ \rightarrow NADH$$

The H^+ and high-energy electrons in the NADH molecules can be used in other chemical reactions or in the production of ATP molecules in the electron-transport chain (described later in this section).

The pyruvic acid and NADH produced in glycolysis can be used in two different biochemical pathways, depending on the availability of O_2. When the amounts of O_2

are limited, anaerobic respiration can take place. Anaerobic respiration does not require O_2 and can quickly produce a few ATP molecules for a short time. If the cell has adequate amounts of O_2, the pyruvic acid and NADH produced in glycolysis are used in aerobic respiration to produce many more ATP.

Anaerobic Respiration

Anaerobic respiration is the breakdown of glucose in the absence of O_2. In human cells, anaerobic respiration results in the production of two molecules of **lactate** and two molecules of ATP (figure 17.6). The ATP thus produced is a source of energy during activities, such as intense exercise, when insufficient O_2 is delivered. Figure 17.6 illustrates the process of anaerobic respiration.

❶ Glucose undergoes several reactions to produce two pyruvic acid molecules, two ATP, and two NADH.

❷ Pyruvic acid is converted to lactic acid, a reaction that requires the input of energy from the NADH produced in glycolysis.

❸ In cells, lactic acid usually releases one H^+ and is converted to **lactate,** the ionized form of lactic acid.

Lactate is released from the cells that produce it, and blood transports it to the liver. When O_2 becomes available, the lactate in the liver can be converted through a series of chemical reactions into glucose. The glucose then can be released from the liver and transported in the blood to cells that use glucose as an energy source. Some of the reactions that convert lactate to glucose require the input of energy derived from ATP that is produced by aerobic respiration. The O_2 necessary to make enough ATP for the synthesis of glucose from lactate contributes to the **oxygen deficit** (see chapter 7).

Aerobic Respiration

Aerobic (ai-ROH-bik) **respiration** is the breakdown of glucose in the presence of O_2 to produce CO_2, water, and 32 molecules of ATP. Figure 17.7 illustrates the process of aerobic respiration.

❶ *Glycolysis*. The six-carbon glucose molecule is broken down to form two molecules of pyruvic acid, each consisting of three carbon atoms. Two ATP (net gain) and two NADH molecules are also produced.

❷ *Acetyl-CoA formation*. Each pyruvic acid moves from the cytoplasm into a mitochondrion, where enzymes remove a carbon atom from the three-carbon pyruvic acid molecule to form CO_2 and a two-carbon acetyl (AS-eh-til) group. Hydrogen ions and electrons are released in the reaction and can be used to produce NADH. Each acetyl group combines with coenzyme A (CoA), derived from vitamin B_2, to form **acetyl-CoA.** Because two pyruvic acid molecules are

produced in phase 1, phase 2 results in two acetyl-CoA molecules, two CO_2 molecules, and two NADH molecules for each glucose molecule.

❸ *Citric acid cycle.* Each acetyl-CoA combines with a four-carbon molecule to form a six-carbon citric acid molecule, which enters the citric acid cycle. The **citric** (SIT-rik) **acid cycle** is also called the *tricarboxylic* (try-kar-BOK-sil-ik) *acid (TCA) cycle* (citric acid has three carboxylic acid groups) or the *Krebs cycle,* after its discoverer, British biochemist Sir Hans Krebs (1900–1981). The citric acid cycle is a series of reactions wherein the six-carbon citric acid molecule is converted, in a number of steps, into a four-carbon molecule. The four-carbon molecule can then combine with another acetyl-CoA molecule to form another citric acid molecule and reinitiate the cycle. During the cycle, two carbon atoms are used to form CO_2, and energy, H^+, and electrons are released. Some of the energy can be used to produce ATP. Most of the energy, H^+, and electrons are used to form NADH molecules and another carrier molecule, called **flavin** (FLA-vin) **adenine dinucleotide ($FADH_2$).** These molecules are used in the electron-transport chain to generate additional ATP. Carbon dioxide diffuses out of the cell and into the blood. It is transported by the circulatory system to the lungs, where it is exhaled. Thus, the carbon atoms that constitute food molecules, such as glucose, are eventually eliminated from the body as CO_2. We literally breathe out part of the food we eat!

❹ *Electron-transport chain.* The **electron-transport chain** is a series of electron-transport molecules attached to the inner mitochondrial membrane. This membrane divides the interior of the mitochondrion into an inner compartment and an outer compartment. Electrons are transferred from NADH and $FADH_2$ to the electron-transport carriers, and H^+ is released into the inner mitochondrial compartment. Some of the electron-transport carriers are also H^+ pumps, which use some of the energy from the transported electrons to pump H^+ from the inner to the outer mitochondrial compartment. Because of an increased H^+ concentration in the outer compartment, the H^+ passes by diffusion back into the inner compartment. The H^+ passes through channels in the inner mitochondrial membrane that couple the movement of the H^+ to ATP production. In the last step of the electron-transport chain, two H^+ and two electrons combine with an O_2 atom to form H_2O:

$$2\,H^+ + 2\,e^- + \tfrac{1}{2}O_2 \rightarrow H_2O$$

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PROCESS Figure

PROCESS Figure 17.7 Aerobic Respiration

Aerobic respiration involves four phases: (1) glycolysis, (2) acetyl-CoA formation, (3) the citric acid cycle, and (4) the electron-transport chain. The number of carbon atoms in a molecule is indicated after the molecule's name. As glucose is broken down, the carbon atoms from glucose are incorporated into carbon dioxide.

Understand

What happens to the CO_2 produced by aerobic respiration?

Without O_2 to accept the H^+ and electrons, the citric acid cycle and the electron-transport chain cannot function. Note that the O_2 we breathe in is eventually bound to two hydrogen atoms to become water, which has many uses in the body (see chapter 2).

Apply

Apply It 4

Many poisons function by blocking certain steps in the metabolic pathways. For example, cyanide blocks the last step in the electron-transport chain. Explain why this blockage causes death.

Summary of Anaerobic Respiration and Aerobic Respiration

In anaerobic respiration, each glucose molecule ($C_6H_{12}O_6$) yields 2 ATP and 2 lactate molecules ($C_3H_6O_3$) through glycolysis:

$$C_6H_{12}O_6 + 2\ ADP + P_i \rightarrow 2\ C_3H_6O_3 + 2\ ATP$$

In contrast, in aerobic respiration, each glucose molecule yields 32 ATP:

$$C_6H_{12}O_6 + 6\ O_2 + 32\ ADP + 32\ P_i \rightarrow 6\ CO_2 + 6\ H_2O + 32\ ATP$$

Of the 32 ATP molecules, 2 result from glycolysis, 2 result from the citric acid cycle, and 28 form through the electron-transport chain. Thus, aerobic respiration is much more efficient at producing ATP than is anaerobic respiration. In addition, many of the chemical reactions of aerobic respiration can be used to produce energy from other food molecules, such as lipids and proteins (see "Lipid Metabolism" and "Protein Metabolism" next).

The number of ATP molecules produced during aerobic respiration can also be reported as 30. The 2 NADH molecules produced by glycolysis cannot cross the inner mitochondrial membrane; thus, their electrons are donated to a shuttle molecule that carries the electrons to the electron-transport chain. The actual number of ATP produced from the glycolytic NADH varies depending on the shuttle molecule used to move the NADH into the mitochondrion. In skeletal muscle and in the brain, fewer ATP molecules are produced for each NADH molecule formed during glycolysis, resulting in a total number of 30 ATP molecules; however, in the liver, kidneys, and heart, more ATP molecules are produced for each NADH molecule, and the total number of ATP molecules formed is 32.

Lipid Metabolism

Triglycerides, or fat, are the body's main energy-storage molecules. In a normal person, fat is responsible for about 99% of the body's energy storage, and glycogen accounts for the remaining 1%.

Between meals, triglycerides in adipose tissue are broken down into fatty acids and glycerol. Some of the fatty acids produced are released into the blood. Other tissues, especially skeletal muscle and the liver, use the fatty acids as a source of energy.

The metabolism of fatty acids takes place in the mitochondria. It occurs by a series of reactions wherein two carbon atoms are removed from the end of a fatty acid chain to form acetyl-CoA (see figure 17.4, *step* 2). As the process continues, carbon atoms are removed two at a time until the entire fatty acid chain is converted into acetyl-CoA. Acetyl-CoA can enter the citric acid cycle and be used to generate ATP. In the liver, two acetyl-CoA molecules can also combine to form **ketones** (KEE-tones). The ketones are released into the blood and travel to other tissues, especially skeletal

muscle. In these tissues, the ketones are converted back to acetyl-CoA, which can enter the citric acid cycle to produce ATP.

The presence of small amounts of ketones in the blood is normal and beneficial, but excessive production of ketones is called **ketosis** (ki-TOH-sis). If the increased number of ketones exceeds the capacity of the body's buffering systems, acidosis, a decrease in blood pH, can occur (see section 18.8, "Regulation of Acid-Base Balance"). Conditions that increase lipid metabolism can increase the rate of ketone formation. Examples are starvation (see the Clinical Impact "Starvation and Obesity" later in this chapter), diets consisting of proteins and fats with few carbohydrates, as well as untreated diabetes mellitus (see chapter 10). Because ketones are excreted by the kidneys and lungs, characteristics of untreated diabetes mellitus include ketones in the urine and "acetone breath."

Protein Metabolism

Amino acids are the products of protein digestion. Once amino acids are absorbed into the body, they are quickly taken up by cells, especially in the liver. Amino acids are used primarily to synthesize needed proteins and only secondarily as a source of energy. If serving as a source of energy, amino acids can be used in two ways (see figure 17.4, *step* 3): (1) The amino acids can be converted into the molecules of carbohydrate metabolism, such as pyruvic acid and acetyl-CoA. These molecules can be metabolized to yield ATP. (2) The amine group ($-NH_2$) can be removed from the amino acid, leaving ammonia and an α-keto acid. This process produces NADH, which can enter the electron-transport chain to produce ATP. Ammonia is toxic to cells, so the liver converts it to urea, which is transported through the blood to the kidneys, where it is eliminated. The α-keto acid can enter the citric acid cycle or can be converted into pyruvic acid, acetyl-CoA, or glucose. Although proteins can serve as an energy source, they are not considered major storage molecules.

Metabolic States

The body experiences two major metabolic states. The first is the **absorptive state,** the period immediately after a meal, when nutrients are being absorbed through the intestinal wall into the circulatory and lymphatic systems (figure 17.8). The absorptive state usually lasts about 4 hours after each meal, and most of the glucose that enters the blood is used by cells for the energy they require. The remainder of the glucose is converted into glycogen or lipids. Most of the absorbed lipids are deposited in adipose tissue. Many of the absorbed amino acids are used by cells in gene expression, and some are used for energy; still other absorbed amino acids enter the liver and are converted to lipids or carbohydrates.

Figure 17.8 **Events of the Absorptive State**

Absorbed molecules, especially glucose, are used as sources of energy. Molecules not immediately needed for energy are stored: Glucose is converted to glycogen or triglycerides, triglycerides are deposited in adipose tissue, and amino acids are converted to triglycerides or carbohydrates.

The second state, the **postabsorptive state,** occurs late in the morning, late in the afternoon, or during the night after each absorptive state is concluded (figure 17.9). Normal blood glucose levels range between 70 and 110 mg/dL, and it is vital to the body's homeostasis that this range be maintained. During the postabsorptive state, blood glucose levels are maintained by the conversion of other molecules to glucose. The first source of blood glucose during the postabsorptive state is the glycogen stored in the liver. However, this glycogen supply can provide glucose for only about four hours. The glycogen stored in skeletal muscles can also be used during vigorous exercise. As the glycogen stores are depleted, the body uses lipids as an energy source. The glycerol from triglycerides can be converted to glucose. The fatty acids can be converted to acetyl-CoA, moved into the citric acid cycle, and used as a source of energy to produce ATP. In the liver, acetyl-CoA can be used to produce ketone bodies that other tissues can use for energy (see figure 17.4). The use of fatty acids as an energy source can partly eliminate the need to use glucose for energy, so that less glucose is removed from the blood and homeostasis is maintained. The amino acids of proteins can be converted to glucose or can be used to produce energy, again sparing blood glucose.

Figure 17.9 **Events of the Postabsorptive State**

Stored energy molecules are used as sources of energy: Glycogen is converted to glucose; triglycerides are broken down to fatty acids, some of which are converted to ketones; and proteins are converted to glucose.

Metabolic Rate

Metabolic rate is the total amount of energy produced and used by the body per unit of time. Metabolic rate is usually estimated by measuring the amount of O_2 used per minute. One liter of O_2 consumed by the body is estimated to produce 4.825 kcal of energy.

Metabolic energy can be used in three ways: (1) for basal metabolism, (2) for muscle contraction, and (3) for the assimilation of food, which involves processes such as the production of digestive enzymes and the active transport of digested molecules. The **basal metabolic rate (BMR)** is the energy needed to keep the resting body functional. It is the metabolic rate calculated in expended kilocalories per square meter of body surface area per hour. BMR is measured when a person is awake but restful and has not eaten for 12 hours. A typical BMR for a 70-kg (154-lb) male is 38 kcal/m^2/hour.

Basal metabolism supports active transport mechanisms, muscle tone, maintenance of body temperature, beating of the heart, and other activities. A number of factors can affect the BMR, such as sex, age, and body temperature. Males have a higher BMR than females, younger people have a higher BMR than older people, and fever can increase BMR. Greatly reduced kilocaloric input, as occurs during dieting or fasting, depresses the BMR.

CLINICAL IMPACT

Starvation and Obesity

Starvation

Starvation is the inadequate intake of nutrients or the inability to metabolize or absorb nutrients. Starvation can be caused by a number of factors, such as prolonged fasting, anorexia, deprivation, or disease.

Symptoms of starvation, in addition to weight loss, include apathy, listlessness, withdrawal, and increased susceptibility to infectious diseases. Few people die directly from starvation because they usually die of an infectious disease first. Other signs of starvation include changes in hair color, flaky skin, and massive edema in the abdomen and lower limbs, causing the abdomen to appear bloated.

During starvation, the body's ability to consume normal volumes of food also decreases. Foods high in bulk but low in protein content often cannot reverse the process of starvation. Intervention involves feeding the starving person low-bulk foods containing ample protein, calories, vitamins, and minerals. Starvation also results in dehydration; thus, rehydration is an important part of intervention. Even with intervention, a victim may be so affected by disease or weakness that he or she cannot recover.

Obesity

Obesity is the storage of excess fat, and it results from the ingestion of more food than is necessary for the body's energy needs. Obesity can be defined on the basis of body weight, body mass index, or body fat. "Desirable body weight" is listed in a table produced by the Metropolitan Life Insurance Company and indicates, for any height, the weight associated with a maximum lifespan. Overweight is defined as 10% more than the desirable weight, and obesity is 20% more than the desirable weight. **Body mass index (BMI)** can be calculated by dividing a person's weight (Wt) in kilograms by the square of his or her height (Ht) in meters:

$$\mathrm{BMI} = \mathrm{Wt} / \mathrm{Ht}^2$$

A BMI greater than 25–27 is overweight, and a value greater than 30 is defined as obese. About 26% of Americans have a BMI of 30 or greater. In terms of the percent of total body weight contributed by fat, 15% body fat in men and 25% body fat in women is associated with reduced health risks. Obesity is defined as more than 25% body fat in men and 30–35% in women.

The distribution of fat in obese individuals can vary. Fat can accumulate mainly in the upper body, such as in the abdominal region, or it can be associated with the hips and buttocks. These distribution differences can be clinically significant because upper body obesity is associated with an increased likelihood of diabetes mellitus, cardiovascular disease, stroke, and death.

In some cases, obesity is caused by a medical condition. For example, a tumor in the hypothalamus can stimulate overeating. In most cases, however, no specific cause can be recognized. In fact, obesity can occur for many reasons and can have more than one cause in the same individual. There seems to be a genetic component for obesity; if one or both parents are obese, their children are more likely to be obese. Environmental factors, such as eating habits, can also play an important role. For example, adopted children can exhibit obesity similar to that of their adoptive parents. In addition, psychological factors, such as overeating as a way to deal with stress, can contribute to obesity.

In **hypertrophic** (high-per-TROF-ik; *hyper-*, above normal + *trophe*¯, nourishment) **obesity,** the number of adipose cells is usually normal, but the amount of lipids contained in each adipose cell is increased. This type of obesity is characteristic of adult-onset obesity. People who were thin or of average weight and quite active when young become less active as they age. Although they no longer use as many kilocalories, they still consume the same amount of food as when they were younger. The excess kilocalories (see "Metabolic Rate" earlier in this section) are used to synthesize fat. In this type of obesity, the amount of lipids in each adipose cell increases, and if the amount of stored lipids continues to increase, the total number of adipose cells may also increase. It is estimated that the average U.S. resident gains 1.25–1.5 lb of body fat per year after age 25 and, at the same time, loses 0.25–0.5 lb of lean body weight (muscle mass) per year.

In **hyperplastic** (high-per-PLAS-tik; *hyper-* + *plasis*, a molding) **obesity,** which is characteristic of juvenile-onset obesity, the number of adipose cells is increased. This condition may also be accompanied by an increase in cell size (hypertrophic obesity). Hyperplastic obesity has a very strong hereditary component, but family eating habits can also have a great influence. People with hyperplastic obesity are obese as

children and become more obese with age. This type of obesity is a major health problem in school-age children.

The daily input of energy should equal the energy demands of metabolism; otherwise, a person will gain or lose weight. For a 23-year-old, 70-kg (154-lb) male to maintain his weight, the input should be 2700 kcal/day; for a 58-kg (128-lb) female of the same age, 2000 kcal/day are necessary. A pound of body fat contains about 3500 kcal. Reducing kilocaloric intake by 500 kcal/day can result in the loss of 1 lb of fat per week. Clearly, adjusting kilocaloric input is an important way to control body weight.

The other way to control weight is through energy expenditure. Physical activity through skeletal muscle movement (exercise) greatly increases the metabolic rate. In the average person, basal metabolism accounts for about 60% of energy expenditure, muscular activity 30%, and assimilation of food about 10%. Of these amounts, energy loss through muscular activity is the only component that a person can reasonably control. Comparing the number of kilocalories gained from food and the number of kilocalories burned during exercise reveals why losing weight is difficult. For example, if brisk walking uses 225 kcal/h, it takes 20 minutes of brisk walking to burn off the 75 kcal in one slice of bread (75/225 = 0.33 h). Research suggests that a combination of appropriate physical activity and appropriate kilocaloric intake is the best approach to maintaining a healthy body composition and weight.

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Apply It 5

If watching TV uses 95 kcal/h, how long does it take to burn off the kilocalories in one cola or beer (see table 17.1)? If jogging at a pace of 6 mph uses 580 kcal/h, how long does it take to use the kilocalories in one cola or beer?

17.3 BODY TEMPERATURE REGULATION

Learning Outcome *After reading this section, you should be able to*

A. Describe heat production and regulation in the body.

Humans can maintain a relatively constant internal body temperature despite changes in the temperature of the surrounding environment. A constant body temperature is very important to homeostasis. For example, environmental temperatures are too low for normal enzyme function. The heat produced by metabolism and muscle contraction helps maintain the body temperature at a steady, elevated level that is high enough for normal enzyme function. Excessively high temperatures can alter enzyme structure, resulting in loss of the enzyme's function.

Free energy is the total amount of energy that can be liberated by the complete catabolism of food. About 40% of the total energy released by catabolism is used to

accomplish biological work, such as anabolism, muscular contraction, and other cellular activities. The remaining energy is lost as **heat.**

Understand ***Apply It 6***

Explain why we become warm during exercise. Why is shivering useful when we are cold?

Normal body temperature is regulated in the same way as other homeostatic conditions in the body. The average normal temperature is usually considered to be 37°C (98.6°F) when measured orally and 37.6°C (99.7°F) when measured rectally. Rectal temperature comes closer to the true core body temperature, but an oral temperature is more easily obtained in older children and adults and therefore is the preferred measure. The normal oral temperature may vary from person to person, with a range of approximately 36.1–37.2°C (97–99°F).

Body temperature is maintained by balancing heat input with heat loss. The body and the environment exchange heat in four ways: (1) radiation, (2) conduction, (3) convection, and (4) evaporation (figure 17.10). **Radiation** is the gain or loss of heat as infrared energy between two objects that are not in physical contact with each other. For example, heat can be gained by radiation from the sun, a hot coal, or the hot sand of a beach. On the other hand, heat can be lost as radiation to cool vegetation, water in the ocean, or snow on the ground. **Conduction** is the exchange of heat between objects that are in direct contact with each other, such as the bottom of the feet and the ground. **Convection** is a transfer of heat between the body and the air or water. A cool breeze moves air over the body and causes loss of heat from the body. **Evaporation** is the conversion of water from a liquid to a gaseous form. As water evaporates from body surfaces, heat is lost.

Figure 17.10 **Heat Exchange**

Heat exchange between a person and the environment occurs by radiation, conduction, convection, and evaporation. *Arrows* show the direction of net heat gain or loss in this environment.

M.M. Sweet/Moment/Getty Images

The amount of heat exchanged between the environment and the body is determined by the difference in temperature between the two. The greater the temperature difference, the greater the rate of heat exchange. Control of the temperature difference can be used to regulate body temperature. For example, if the environmental temperature is very cold, as occurs on a winter day, there is a large temperature difference between the body and the environment, and therefore a large loss of heat. Behaviorally, we can reduce the loss of heat by selecting a warmer environment, such as by going inside a heated house or by putting on extra clothes. Physiologically, the body controls the temperature difference through dilation and constriction of blood vessels in the skin. When the blood vessels dilate, they bring warm blood to the surface of the body, raising skin temperature; when the blood vessels constrict, blood flow and skin temperature decrease (see figure 5.9).

Understand

Apply It 7

Explain why constriction of skin blood vessels on a cold winter day is beneficial.

When environmental temperature is greater than body temperature, dilation of blood vessels in the skin brings blood to the skin, causing an increase in skin temperature that decreases the gain of heat from the environment. At the same time, evaporation carries away excess heat to prevent heat gain and overheating.

Body temperature regulation is an example of a negative-feedback system (figure 17.11). Maintenance of a specific body temperature is accomplished by neurons in the hypothalamus, which regulate body temperature around a set point. A small area in the anterior part of the hypothalamus can detect slight increases in body temperature through changes in blood temperature. As a result, mechanisms that cause heat loss, such as dilation of blood vessels in the skin and sweating, are activated, and body temperature decreases. A small area in the posterior hypothalamus can detect slight decreases in body temperature and can initiate heat gain by increasing muscular activity (shivering) and by initiating constriction of blood vessels in the skin.

Homeostasis Figure 17.11 **Temperature Regulation**

(1) Body temperature is within normal range. (2) Body temperature increases outside the normal range, which causes homeostasis to be disturbed. (3) Receptors in the skin and hypothalamus detect the increase in body temperature and the control center in the hypothalamus responds to the change in body temperature. (4) The effectors are activated. Blood vessels in the skin dilate and sweating increases to promote heat loss and evaporative cooling. (5) Body temperature decreases. (6) Body temperature returns to its normal range, and homeostasis is restored.

Under some conditions, the hypothalamus set point is actually changed. For example, during a fever, the set point is raised. Heat-conserving and heat-producing

mechanisms are stimulated, and body temperature increases. To recover from a fever, the set point is reduced to normal, heat loss mechanisms are initiated, and body temperature decreases.

CLINICAL IMPACT

Too Hot or Too Cold

Hyperthermia is a condition in which heat gain in the body exceeds heat loss. Hyperthermia can result from exposure to a hot environment, exercise, or fever. Prolonged exposure to a hot environment can lead to **heat exhaustion,** in which normal temperature reduction mechanisms cannot keep pace with the excessive environmental heat, thus allowing the body temperature to rise. Heat exhaustion is characterized by cool, wet skin due to heavy sweating. Weakness, dizziness, and nausea usually occur as well. The heavy sweating can lead to dehydration, decreased blood volume, decreased blood pressure, and increased heart rate. Treatment involves increasing heat loss by moving the person to a cooler environment, decreasing heat production by decreasing muscular activity, and replacing lost body fluids. **Heat stroke** results from an increase in the hypothalamic set point and is characterized by dry, flushed skin because sweating is inhibited. The person becomes confused and irritable, and can even become comatose. Treatment is the same as for heat exhaustion but also involves increasing evaporation from the skin by applying water to the skin or by placing the person in cool water.

Hypothermia is a condition in which heat loss exceeds heat gain. The body's normal temperature increase mechanisms are working, but they cannot keep pace with heat loss, and the body temperature decreases. Hypothermia usually results from prolonged exposure to a cold environment or even to a cool, damp environment because the moisture draws heat away from the body. Treatment for hypothermia calls for rewarming the body at a rate of a few degrees per hour. **Frostbite** is local damage to the skin or deeper tissues resulting from prolonged exposure to a cold environment. The best treatment for frostbite is immersion in a warm-water bath. Rubbing the affected area and applying local, dry heat should be avoided.

SUMMARY

17.1 Nutrition

Nutrition is the ingestion and use of food.

Nutrients

1. Nutrients, the chemicals used by the body, consist of carbohydrates, lipids, proteins, vitamins, minerals, and water.

2. Essential nutrients either cannot be produced by the body or cannot be produced in adequate amounts.
3. The MyPlate icon provides a visual reminder for making choices at mealtime, by selecting healthy foods from five food groups. Half the meal should be fruits and vegetables.

Kilocalories

A kilocalorie is the energy required to raise the temperature of 1000 g of water 1°C. A kilocalorie (Calorie) is the unit of measurement used to express the energy content of food.

Carbohydrates

1. Carbohydrates include monosaccharides, disaccharides, and polysaccharides.
2. Most of the carbohydrates we ingest are from plants.
3. Carbohydrates are used as an energy source and for making DNA, RNA, and ATP.
4. The Acceptable Macronutrient Distribution Range (AMDR) for carbohydrates is 45–65% of total kilocalories.

Lipids

1. Lipids include triglycerides, steroids, phospholipids, and fat-soluble vitamins. Triglycerides are a major source of energy. Eicosanoids are involved in inflammation, tissue repair, and smooth muscle contraction. Cholesterol and phospholipids are part of the cell membrane. Some steroid hormones regulate the reproductive system.
2. The AMDR for lipids is 20–35%.

Proteins

1. Proteins are chains of amino acids.
2. Animal proteins tend to be complete proteins, whereas plant proteins tend to be incomplete.
3. Proteins are involved in structural strength, muscle contraction, regulation, buffering, clotting, transport, ion channels, receptors, and the immune system.
4. The AMDR for protein is 10–35% of total kilocalories.

Vitamins

1. Most vitamins are not produced by the body and must be obtained in the diet. Some vitamins can be formed from provitamins.

2. Vitamins are important in energy production, nucleic acid synthesis, growth, and blood clotting.
3. Vitamins are classified as either fat-soluble or water-soluble.
4. Recommended dietary allowances (RDAs) are a guide for estimating the nutritional needs of groups of people on the basis of their age, their gender, and other factors.

Minerals

Minerals are essential for normal metabolic functions. They are involved with establishing the resting membrane potential; generating action potentials; adding mechanical strength to bones and teeth; combining with organic molecules; and acting as coenzymes, buffers, or regulators of osmotic pressure.

Daily Values

1. Daily Values are dietary references that can be used to plan a healthful diet.
2. Daily Values for vitamins and minerals are based on Reference Daily Intakes (RDIs), which are generally the highest 1968 RDA value of an age category.
3. Daily Values are based on Daily Reference Values. The Daily Reference Values for energy-producing nutrients (carbohydrates, total fat, saturated fat, and proteins) and dietary fiber are recommended percentages of the total kilocalories ingested daily for each nutrient. The Daily Reference Values for total fats, saturated fats, cholesterol, and sodium are the uppermost limits considered desirable because of their link to diseases.
4. The % Daily Value is the percentage of the recommended Daily Value of a nutrient found in one serving of a particular food.

17.2 Metabolism

1. Metabolism consists of catabolism and anabolism. Catabolism, the breakdown of molecules, gives off energy. Anabolism, the synthesis of molecules, requires energy.
2. The energy in carbohydrates, lipids, and proteins is used to produce ATP.
3. The energy from ATP can be used for active transport, muscle contraction, and the synthesis of molecules.

Regulation of Metabolism

1. A biochemical pathway is a series of chemical reactions, some of which release energy that can be used to synthesize ATP.
2. Each step in a biochemical pathway requires enzymes.
3. Enzyme synthesis is determined by DNA. Enzyme activity is modified by receptor-mediated and end-product processes.

Carbohydrate Metabolism

1. Glycolysis is the breakdown of glucose to two pyruvic acid molecules. A net yield of Two ATP molecules are also produced.
2. Anaerobic respiration is the breakdown of glucose in the absence of oxygen to two lactate molecules and two ATP molecules.
3. Lactate can be converted to glucose using aerobically produced ATP; the necessary oxygen contributes to the oxygen deficit.
4. Aerobic respiration is the breakdown of glucose in the presence of oxygen to produce carbon dioxide, water, and 32 molecules of ATP. The first phase of aerobic respiration is glycolysis; the second phase is the conversion of pyruvic acid to acetyl-CoA; the third phase is the citric acid cycle; and the fourth phase is the electron-transport chain, which uses carrier molecules, such as NADH, to synthesize ATP.

Lipid Metabolism

1. Lipids are broken down in adipose tissue, and fatty acids are released into the blood.
2. Fatty acids are taken up by cells and broken down into acetyl-CoA, which can enter the citric acid cycle. Acetyl-CoA can also be converted into ketones by the liver. Ketones released from the liver into the blood are used as energy sources by other cells.

Protein Metabolism

1. Amino acids are used to synthesize proteins.
2. Amino acids can be used for energy, yielding ammonia as a by-product. Ammonia is converted to urea and excreted by the kidneys.

Metabolic States

1. In the absorptive state, nutrients are used as energy, with the remainder being stored.
2. In the postabsorptive state, stored nutrients are used for energy.

Metabolic Rate

1. The metabolic rate is the total energy expenditure per unit of time.
2. Metabolic energy is used for basal metabolism, muscular activity, and the assimilation of food.

17.3 Body Temperature Regulation

1. Body temperature is a balance between heat gain and heat loss.
2. Heat is produced through metabolism.
3. Heat is exchanged through radiation, conduction, convection, and evaporation.
4. The greater the temperature difference, the greater the rate of heat exchange.

5. Body temperature is maintained around a set point by neural circuits in the hypothalamus.
6. Dilation of blood vessels in the skin and sweating increase heat loss from the body.
7. Constriction of blood vessels in the skin and shivering promote heat gain by the body.

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REMEMBERING AND UNDERSTANDING

1. Define a nutrient, and list the six major classes of nutrients. What is an essential nutrient?
2. What is a kilocalorie (Calorie)? Distinguish between a Calorie and a calorie.
3. List some sources of carbohydrates, lipids, and proteins in the diet.
4. List the recommended consumption amounts of carbohydrates, lipids, and proteins.
5. What are vitamins and provitamins? Name the water-soluble vitamins and the fat-soluble vitamins. List some of the functions of vitamins.
6. What are the Recommended Dietary Allowances (RDAs)?
7. List some of the minerals, and give their functions.
8. What are the Daily Values? How are the Daily Values related to total daily kilocaloric intake? Why are some Daily Values considered the uppermost amounts that should be consumed?
9. Define a % Daily Value.
10. Define a biochemical pathway. How are the steps in a biochemical pathway controlled? What are three ways in which enzymes are regulated?
11. Describe glycolysis. What molecule is the end product of glycolysis? How many ATP and NADH molecules are produced?
12. What determines whether the pyruvic acid produced in glycolysis becomes lactate or acetyl-CoA?
13. Describe the two phases of anaerobic respiration. How many ATP molecules are produced? What happens to the lactate produced when oxygen becomes available?
14. Define aerobic respiration, and state how many ATP molecules are produced.
15. Describe the citric acid cycle.

16. What is the function of the electron-transport chain?
17. What happens to the carbon atoms in ingested food during metabolism? What happens to the oxygen we breathe in during metabolism?
18. Describe the events occurring during the absorptive and postabsorptive metabolic states.
19. What is meant by metabolic rate? Name three ways that the body uses metabolic energy.
20. Describe how heat is produced by and lost from the body. How is body temperature regulated?

CRITICAL THINKING

1. One serving of a food contains 2 g of saturated fat. What % Daily Value for saturated fat would appear on the food label? (See the bottom of figure 17.2*a* for information needed to answer this question.)
2. An active teenage male consumes 3000 kcal/day. What is the maximum amount (weight) of total fats he should consume, according to the % Daily Values?
3. If the teenager in question 2 eats a food that has a total fat content of 10 g/serving, what is his total fat % Daily Value?
4. Suppose the food in question 3 is in a package that lists a serving size of ½ cup, with four servings in the package. If the teenager eats half the contents of the package (1 cup), how much of his % Daily Value does he consume?
5. Why can some people lose weight on a 1200 kcal/day diet, whereas other people cannot?
6. Sandra, a bodybuilder, wanted to increase her muscle mass. Knowing that proteins are the main components of muscle, she consumed large amounts of protein daily (high-protein diet), along with small amounts of lipids and carbohydrates. Explain why this strategy will or will not work.
7. After consuming a high-protein diet for several days, does a person's urine contain less, the same amount of, or more urea than before she consumed the proteins? Explain.
8. Thyroid hormone is known to increase the activity of the sodium-potassium exchange pump, which is an active-transport mechanism, thereby increasing the breakdown of ATP. If a person produced excess amounts of thyroid hormone, what effect would this have on basal metabolic rate, body weight, and body temperature? How might the body attempt to compensate for the changes in body weight and temperature?
9. On learning that sweat evaporation results in the loss of calories, an anatomy and physiology student decides that sweating is an easier way to lose weight than dieting. He knows that a liter (about a quart) of water weighs 1000 g, which is equivalent to 580,000 cal (or 580 kcal) of heat when lost as sweat. He believes that instead of reducing his

caloric intake by 580 kcal/day, he can lose about a pound of fat a week by losing a liter of sweat every day in the sauna. Will this approach work? Explain.

10. It is recommended that a person on a diet drink six to eight glasses of cool water per day. How could this practice aid weight loss?
11. In some diseases, an infection results in a high fever. The patient is on the way to recovery when the crisis is over and body temperature begins to return to normal. If you were looking for symptoms in a patient who had just passed through the crisis state, would you look for a dry, pale skin or a wet, flushed skin? Explain.

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

18

Urinary System and Fluid Balance

The kidneys employ a complex series of processes to filter our blood of toxins and to conserve water.

LEARN TO APPLY IT

Baby Maya was born early one morning. On her first day home from the hospital, Maya's parents noticed that her diapers were excessively wet hour after hour throughout the day and night. In addition, Maya was irritable, had a slight fever, and had vomited even though she had not eaten for several feedings. Her parents took her to the pediatrician, who ordered blood tests. The tests indicated that Maya had normal levels of antidiuretic hormone (ADH).

After reading this chapter, suggest the underlying mechanism for Maya's disorder.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 13 Urinary System

18.1 FUNCTIONS OF THE URINARY SYSTEM

Learning Outcomes

After reading this section, you should be able to

A. List the structures that make up the urinary system.

B. List the major functions of the urinary system.

The **urinary** (YOOR-i-nair-ee) **system** is the major excretory system of the body. Some organs in other systems also eliminate wastes, but they are not able to compensate in case of kidney failure. The urinary system consists of two kidneys, the primary excretory organs. Each kidney's waste products are carried by a ureter to a single urinary bladder. The waste is emptied from the urinary bladder by the urethra (figure 18.1). The kidneys each filter a large volume of blood. Wastes from the blood are collected and form urine. Urine consists of (1) excess water, (2) excess ions, (3) metabolic wastes, including the protein by-product urea, and (4) toxic substances.

Figure 18.1 APR **Urinary System**

The urinary system consists of two kidneys, two ureters, the urinary bladder, and the urethra.

The kidneys can suffer extensive damage and still maintain homeostasis. As long as about one-third of one kidney remains functional, survival is possible. However, if the functional ability of the kidneys fails completely, death will result unless the person receives medical treatment.

The major function of the urinary system is excretion, which controls the composition and volume of body fluids. The kidneys also have many other important metabolic activities. The kidney functions include:

1. *Excretion.* The kidneys remove waste products from the blood. Most of the waste products are metabolic by-products of cell metabolism. Other waste products are substances absorbed from the intestine. Many waste products are toxic. Organs such as the skin, liver, lungs, and intestines eliminate some of these waste products.

However, if the kidneys fail to function, these organs cannot remove sufficient wastes to maintain homeostasis.

2. *Regulation of blood volume and pressure.* The kidneys play a major role in controlling the extracellular fluid volume in the body. The kidneys can produce either a large volume of dilute urine or a small volume of concentrated urine, depending on the hydration level of the body. Through urine production, the kidneys regulate blood volume and blood pressure.
3. *Regulation of blood solute concentrations.* The kidneys help regulate the concentration of the major molecules and ions, such as glucose, Na^+, Cl^-, K^+, Ca^{2+}, HCO_3^-, and HPO_4^{2-}.
4. *Regulation of extracellular fluid pH.* The kidneys excrete variable amounts of H^+ to help regulate extracellular fluid pH.
5. *Regulation of red blood cell synthesis.* The kidneys secrete a hormone, erythropoietin, which regulates the synthesis of red blood cells in bone marrow (see chapter 11).
6. *Regulation of vitamin D synthesis.* The kidneys play an important role in controlling blood levels of Ca^{2+} by regulating the synthesis of vitamin D (see chapter 6).

18.2 ANATOMY OF THE KIDNEYS

Learning Outcomes *After reading this section, you should be able to*

A. Describe the location and anatomy of the kidneys.

B. Describe the structure of the nephron and the location of the parts of the nephron in the kidney.

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Location and External Anatomy of the Kidneys

The **kidneys** are behind the peritoneum, or **retroperitoneal** (RE-troh-PER-i-toh-NEE-uhl; see chapter 1) and are located on each side of the vertebral column (figure 18.2). They are bean-shaped organs, each about the size of a tightly clenched fist. A layer of connective tissue called the **renal** (derived from the Latin word for kidney) **capsule** surrounds each

kidney. Around the renal capsule is a thick layer of adipose tissue, which protects the kidney from mechanical shock. On the medial side of each kidney is the **hilum** (HIGH-lum), where the renal artery and nerves enter and where the renal vein, ureter, and lymphatic vessels exit the kidney (figure 18.3). The hilum opens into a cavity called the **renal sinus,** which contains blood vessels, part of the system for collecting urine, and adipose tissue.

Figure 18.2 APR **Anatomy of the Urinary System**

(*a*) The kidneys are located in the abdominal cavity, with the right kidney just below the liver and the left kidney below the spleen. A ureter extends from each kidney to the urinary bladder within the pelvic cavity. An adrenal gland is located at the superior pole of each kidney. (*b*) The kidneys are located behind the parietal peritoneum, surrounded by adipose tissue. A connective tissue layer, the renal fascia, anchors the kidney to the abdominal wall. The renal arteries extend from the abdominal aorta to each kidney, and the renal veins extend from the kidneys to the inferior vena cava.

Figure 18.3 APR **Longitudinal Section of the Kidney**

(*a*) The cortex and the medulla of the kidney surround the renal sinus. The renal sinus is a space containing the renal pelvis, calyces, blood vessels, adipose tissue, and other connective tissues. The renal pyramids extend from the cortex of the kidney to the renal sinus. The tip of each renal pyramid is surrounded by a calyx. The calyces connect to the renal pelvis. Urine flows from the tip of the renal pyramid through the calyx and renal pelvis into the ureter. (*b*) Photograph of a longitudinal section through a human kidney.

(b) Rebecca Gray/McGraw-Hill Education

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Internal Anatomy and Histology of the Kidneys

To fully appreciate the function of the kidneys, we must first understand their ultrastructure. The kidneys are organized into two major regions: (1) an outer **cortex** and (2) an inner **medulla** that surrounds the renal sinus (figure 18.3). The cortex is the location for the blood-filtering structures of the kidney. These are discussed in more detail in the next section. The medulla is composed of many cone-shaped structures called **renal pyramids,** whose bases project into the cortex.

The renal pyramids are a collection of tubes and ducts that transport fluid throughout the kidney and modify it into urine. Once urine is formed, ducts in the renal pyramids transport it toward the renal sinus. The tips of the pyramids, the **renal papillae,** point toward the renal sinus. In the renal sinus, another set of tubes collects the urine for movement to the urinary bladder. When urine leaves a renal papilla, it empties into a small, funnel-shaped chamber surrounding the tip of the papilla called a **calyx** (KAY-licks; pl. calyces pronounce). Urine from several calyces is emptied into a single, enlarged, funnel-shaped chamber called the **renal pelvis.** The renal pelvis is embedded in and surrounded by the renal sinus. At the hilum, it narrows significantly, forming the small-diameter tube called the **ureter.** Urine moves from the renal pelvis into the ureter for transport to the urinary bladder. Urine flow is illustrated in figure 18.4.

Figure 18.4 **Urine Flow**

Urine is formed in the cortex and medulla and enters the calyces from the tips of the renal pyramids. From the calyces, urine flows into the renal pelvis and then exits the pelvis through the ureter. Urine flows through the ureters to the bladder, where it is stored. When the urine is released from the bladder, it exits through the urethra into the external environment.

Structure of a Nephron

The **nephron** (NEF-ron; Greek for kidney) is the histological and functional unit of the kidney (figure 18.5). It consists of specialized structures including small tubes that are called tubules. There are approximately 1.3 million nephrons distributed throughout the cortex and medulla of each kidney. The four regions of a nephron are: (1) a **renal corpuscle,** (2) a **proximal convoluted tubule,** (3) a **loop of Henle,** and (4) a **distal convoluted tubule.** Each portion of a nephron plays a different role in urine production. Generally speaking, the renal corpuscle filters the blood, the proximal convoluted tubule returns filtered substances to the blood, the loop of Henle helps conserve water and solutes, and the distal convoluted tubule rids the blood of additional wastes. The fluid in the distal convoluted tubule then empties into a collecting duct, which carries the newly formed urine from the cortex of the kidney toward the renal papilla deep in the medulla. Near the tip of the renal papilla, several collecting ducts merge into a larger-diameter tubule called a **papillary duct,** which empties into a calyx.

Figure 18.5 **Functional Unit of the Kidney—the Nephron**

A nephron consists of a renal corpuscle, a proximal convoluted tubule, a loop of Henle, and a distal convoluted tubule. The distal convoluted tubule empties into a collecting duct. Juxtamedullary nephrons (those near the medulla of the kidney) have loops of Henle that extend deep into the medulla of the kidney, whereas cortical nephrons do not. Collecting ducts merge into larger papillary ducts, which empty into a calyx.

Types of Nephrons

There are two types of nephrons in the kidney: (1) juxtamedullary nephrons and (2) cortical nephrons. **Juxtamedullary** (JUKS-ta-MED-u-lair-ee; next to medulla) nephrons have renal corpuscles that are found deep in the cortex near the medulla. They have long loops of Henle, which extend deep into the medulla. Longer loops of Henle are well adapted for water conservation (see section 18.3). Only about 15% of nephrons are juxtamedullary nephrons.

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Cortical nephrons have renal corpuscles that are distributed throughout the cortex. Their loops of Henle are shorter than those of juxtamedullary nephrons and are closer to the outer edge of the cortex (figure 18.5).

The Renal Corpuscle

The filtration portion of the nephron is housed in the renal corpuscle. The renal corpuscle consists of (1) the glomerulus and (2) the Bowman capsule. The **glomerulus** (glo-MER-you-lus; ball of yarn) is a network of capillaries twisted around each other like a ball of yarn (figure 18.6*a,b*). Fcrular capillaries is called the filtrate. The **Bowman capsule,** or *glomerular capsule,* is an indented, double-walled chamber surrounding the glomerulus. From the Bowman capsule, the filtered fluid flows into the proximal convoluted tubule region of the renal tubule.

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(a) The renal corpuscle consists of the Bowman capsule and the glomerulus. The Bowman capsule is the enlarged end of a nephron, which is indented to form a double-walled chamber. The Bowman capsule surrounds the glomerulus, which is a network of capillaries. Blood flows from the afferent arteriole into the glomerulus and leaves the glomerulus through the efferent arteriole.

(b) The visceral layer of the Bowman capsule covers the glomerular capillaries. Fluid from the blood enters the Bowman capsule by passing through the capillary walls and the visceral layer of the Bowman capsule. From there, fluid passes into the proximal convoluted tubule of the nephron. The juxtaglomerular apparatus consists of cells from the wall of the afferent arteriole and the distal convoluted tubule.

(c) The glomerulus is composed of porous capillaries. The visceral layer of the Bowman capsule consists of specialized cells called podocytes.

(d) The filtration membrane consists of the porous glomerular capillary endothelium, a basement membrane, and the podocyte cell processes. Fluid passes from the capillary through the filtration membrane into the Bowman capsule.

Figure 18.6 APR **Renal Corpuscle and Filtration Membrane**

Filtration of the blood occurs in the renal corpuscle.

A Bowman capsule consists of two layers: (1) an outer layer and (2) an inner layer (figure 18.6*b*). The outer layer is constructed of simple

squamous epithelial cells. The epithelial cells become cube-shaped at the beginning of the proximal convoluted tubule. The inner layer is constructed of specialized cells called **podocytes,** which wrap around the glomerular capillaries.

The renal corpuscle has several unique characteristics that make it particularly efficient at filtration—the main function of the kidneys.

1. *Porous capillaries.* The glomerular capillaries are highly permeable due to the presence of pores. Capillaries have different levels of permeability, depending on the size of their pores. In the case of the glomerular capillary pores, neither large proteins nor blood cells can fit through them.
2. *Porous inner layer of Bowman capsule.* There are gaps between the cell processes of the podocytes of the inner layer (figure 18.5*c*). A basement membrane lies sandwiched between the endothelial cells of the glomerular capillaries and the podocytes of the Bowman capsule.
3. *High pressure.* An **afferent** (AF-eh-rent; *aff,* toward) **arteriole** supplies blood to the glomerulus for filtration. An **efferent** (EF-eh-rent; *eff,* away from) **arteriole** transports the filtered blood away from the glomerulus (figure 18.6*a*). The glomerular capillaries have much higher pressure than other capillaries due to the smaller diameter of the efferent arteriole compared to the afferent arteriole.

Together, the structures in the corpuscle make up the filtration membrane. The filtration membrane consists of capillary endothelium, the basement membrane, and the podocytes of the Bowman capsule (figure 18.6*d*). We will discuss the filtration membrane in greater detail in section 18.3. The filtration membrane performs the first major step in urine production. Urine production begins when the filtration membrane filters the blood. The filtered fluid, called **filtrate,** then enters the lumen, or space, inside the Bowman capsule.

An important regulatory structure, called the **juxtaglomerular apparatus**, is located next to the glomerulus (figure 18.6*b*).

The juxtaglomerular apparatus consists of a unique set of afferent arteriole cells and specialized cells in the distal convoluted tubule that are in close contact with each other. These specialized cells include the following:

1. At the point where the afferent arteriole enters the renal corpuscle, it has a cuff of specialized smooth muscle cells around it. These cells are called **juxtaglomerular cells.**
2. A part of the distal convoluted tubule of the nephron lies between the afferent and efferent arterioles next to the renal corpuscle. In this section of the distal convoluted tubule, there is a group of specialized cells called the **macula** (MAK-you-lah) **densa.**

Secretion of the enzyme renin by the juxtaglomerular apparatus plays an important role in the regulation of filtrate formation and blood pressure (see section 18.4).

The Renal Tubule

Once the blood is filtered, the resulting fluid is modified to form urine as it passes through each section of the renal tubule. The first section is the **proximal convoluted tubule**. The wall of the proximal convoluted tubule is composed of simple cuboidal epithelium. These cells have many microvilli, which serves to increase the surface area of these cells.

As the proximal convoluted tubule continues descending toward the medulla, the cell type begins to change. At this point the renal tubule is called the **loop of Henle**. Every loop of Henle has two limbs: (1) the **descending limb** and (2) the **ascending limb.** The first part of the descending limb is similar in structure to the proximal convoluted tubule. The portion of the loop of Henle that extends into the medulla becomes very thin near the bend of the loop. The lumen in the thin part narrows, and an abrupt transition occurs from simple cuboidal epithelium to simple squamous epithelium. Like the descending limb, the first part of the ascending limb is thin and made of simple squamous epithelium. Soon, however, it becomes thicker, and simple cuboidal epithelium replaces the simple squamous epithelium. The thick part of the ascending limb returns toward the renal corpuscle and ends by transitioning to the distal convoluted tubule near the macula densa.

The **distal convoluted tubule** is shorter than the proximal convoluted tubule. Its epithelium is simple cuboidal. However, these cells are smaller

and have fewer microvilli. Several distal convoluted tubules connect to a single **collecting duct,** which is composed of simple cuboidal epithelium. The collecting duct, which is larger in diameter than the segments of the nephron, extends through the medulla toward the tips of the renal pyramids.

Arteries and Veins

A system of blood vessels allows the exchange of materials that occurs in the kidneys. The **renal arteries** branch off the abdominal aorta and enter the kidneys (figure 18.7*a*). As the renal artery extends deep into the kidney, it branches into smaller and smaller blood vessels. The following is a list of blood vessels, in order, starting with the renal artery and progressing to the blood vessels that surround each nephron.

1. The **interlobar** (in-ter-LOH-bar; between the lobes) **arteries** pass between the renal pyramids.
2. The **arcuate** (AR-kyu-ate; arched) **arteries** branch from the interlobar arteries. They arch between the cortex and the medulla.
3. **Interlobular arteries** branch off the arcuate arteries and project into the cortex.
4. The **afferent arterioles** arise from branches of the interlobular arteries. The afferent arterioles carry blood to the glomerular capillaries (figure 18.7*b*).
5. **Efferent arterioles** carry blood from the glomerular capillaries.
6. The **peritubular** (around the tubes) **capillaries** branch from the efferent arterioles. They surround the proximal convoluted tubules, the distal convoluted tubules, and the loops of Henle. The **vasa recta** (VAH-sah REK-tah; straight vessels) are specialized portions of the peritubular capillaries that extend deep into the medulla of the kidney and surround the loops of Henle and collecting ducts.

Figure 18.7 APR **Blood Flow Through the Kidney**

(*a*) Blood flow through the larger arteries and veins of the kidney. Vessels are listed in order from entry of blood into the kidney to exit of blood from the kidney. (*b*) Blood flow through the arteries, capillaries, and veins that provide circulation to the nephrons. Vessels are listed in order from blood flowing into the glomerulus and blood exiting the nephron circulation. (*c*) Blood flow pathway from entry into the kidney and through vessels of the nephron.

Blood from the peritubular capillaries, including the vasa recta, will return to the general circulation through the veins of the kidneys (figure 18.7). Figure 18.7*c* summarizes the blood flow through the kidney.

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18.3 URINE PRODUCTION

Learning Outcomes ***After reading this section, you should be able to***

A. Identify the principal factors that influence filtration pressure.

B. Explain how the factors influencing filtration affect the rate of filtrate production.

C. Give the function of the proximal convoluted tubule, descending and ascending limbs of the loop of Henle, distal convoluted tubule, and collecting duct

D. Explain how the movement of substances across the wall of the nephron and collecting duct influences the composition of the filtrate.

The primary function of the kidney is regulation of body fluid composition. The kidney is the organ that sorts the substances from the blood for either removal in the urine or return to the blood. Substances that are waste products, toxins, and excess materials are permanently removed from the body, whereas other substances need to be conserved to maintain homeostasis. The structural components that perform this sorting are the nephrons, the functional units of the kidney. If you have ever decided to organize your "junk" drawer in your desk or kitchen, you may realize just how difficult it is to quickly sort through all its contents. In fact, you may have found yourself simply emptying the drawer onto a table and then sorting the contents one by one as you place objects into a "save" group or a "throw away" group. In a sense, the kidney uses the same approach when regulating blood composition. The "throw away" items end up in the urine, and the "save" items go back into the blood. Urine is mostly water and some organic waste products, as well as excess ions (table 18.1).

TABLE 18.1 The Average Concentration of Major Urine Substances

Substance	Plasma	Urine
Water (L/day)		1.4
Organic molecules (mg/dL)		
Protein	3900–5000	0*
Glucose	100	0
Urea	26	1820
Uric acid	3	42
Creatinine	1	196
Ions (mEq/L)		
Na^+	142	128
K^+	5	60
Cl–	103	134
HCO_3^-	28	14
Specific gravity (g/ml)†	1.019–1.022	1.005–1.030
pH	7.35–7.45	4.5–8.0

*Trace amounts of protein can be found in the urine.
†The specific gravity increases as the concentration of solutes in urine increases.

Scientists usually categorize urine formation into three major processes: (1) filtration, (2) tubular reabsorption, and (3) tubular secretion. Figure 18.8 illustrates the location of each of these processes within the kidney.

❶ **Filtration.** Blood pressure in the glomerular capillaries forces fluid and small molecules out of the blood to create filtrate. Filtration is nonselective and separates based only on size or charge of molecules. Filtration is comparable to emptying your "junk" drawer of everything except large, permanent items. Filtration does not remove everything in the blood. Filtration removes only those substances small enough to fit through the filtration membrane.

❷ **Tubular reabsorption.** Cells in the renal tubules contain many transport proteins. These transport proteins move water and some filtered molecules from the filtrate back into the blood in the peritubular capillaries. This prevents them from being lost from the body as components of urine (these are the "saved" items from your junk drawer). Most of the filtered water and useful solutes have been returned to the blood by the time the filtrate has been modified to urine, whereas the remaining waste or excess substances, and a small amount of water, form urine (table 18.1).

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❸ **Tubular secretion.** Certain tubule cells transport additional solutes from the blood into the filtrate. Some of these solutes may not have been filtered by the filtration membrane (these are some "throw away" items that had been left behind in your junk drawer).

PROCESS Figure

PROCESS Figure 18.8 **Urine Formation**

Urine formation involves three major processes. Filtration occurs within the renal corpuscle. Reabsorption happens primarily in the proximal convoluted tubule and the loop of Henle although there is some reabsorption in the distal convoluted tubule. Secretion occurs mostly in the distal convoluted tubule, but may also occur in the proximal convoluted tubule.

What would happen to water reabsorption if the osmotic pressure of the blood were to increase above normal?

Urine consists of substances filtered directly from the blood and those that are secreted into the renal tubule, minus any reabsorbed substances.

Filtration

Filtration is a nonspecific process whereby materials are separated based on size or charge. A simple example of size filtration is demonstrated by a drip coffeemaker. In this case, the driving force of filtration is gravity. The kidneys also use size filtration to remove substances from the blood by filtering it, but in this case, the driving force of this filtration is blood pressure. The importance of filtration is indicated by the large percentage of blood that is sent through the kidneys compared with other organs.

An average of 21% of the blood pumped by the heart each minute flows through the kidneys. Of the total volume of blood plasma that flows through the glomerular capillaries, about 19% passes through the filtration membrane into the Bowman capsule to become filtrate. In all the nephrons of both kidneys, about 180 liters (L) of filtrate are produced each day, but only about 1% or less of the filtrate becomes urine because most of the filtrate is reabsorbed. The formation of such a large volume of filtrate allows toxins to be quickly removed from the blood.

Recall that the renal corpuscles in the renal cortex contain the filtration structures, each of which is called a **filtration membrane.** The membrane separates materials on the basis of size and charge of the blood components. Thus, the filtration membrane allows water and small molecules to leave the blood while preventing blood cells and most proteins from leaving the blood. Several structures make up the filtration membrane:

1. The porous glomerular capillaries
2. The basement membrane between the capillary wall and the visceral layer of the Bowman capsule
3. Podocytes of the inner layer of the Bowman capsule (see figure 18.6*d*)

Together, these components prevent many larger molecules from entering the filtrate. For example, antibody molecules are too large to pass through, but glucose and amino acids can pass through the filtration membrane into the filtrate. Most plasma proteins are too large to be filtered out of the blood and are retained in the glomerular capillaries. However, albumin, a smaller protein, and some small protein hormones are able to enter the filtrate, but only in small amounts. Therefore, the filtrate is not protein-free, but it only contains about 0.1% protein or less. However, because cells in the proximal convoluted tubule return filtered glucose, amino acids, and proteins to the blood, the urine of healthy individuals does not contain glucose or amino acids, and contains only a very small amount of protein. We will discuss reabsorption in the proximal convoluted tubule in the next section.

Filtration Pressure

Filters differ in the sizes of the elements they filter, but they all have one thing in common: Each requires a force to cause movement through it. For example, for a coffee maker, as noted earlier, the force is gravity. For the filtration membrane, three forces, or pressures, determine the amount of filtrate formed. The combination of these three pressures is called **filtration pressure.** Figure 18.9 illustrates the source of the three pressures contributing to filtration pressure.

PROCESS Figure

PROCESS Figure 18.9 Filtration Pressure

The principal force for filtration is glomerular capillary pressure.

Suppose a person consumed a high-protein diet. What effect might this have on filtration pressure and urine volume?

❶ **Glomerular capillary pressure.** The glomerular capillary pressure is essentially the blood pressure inside the glomerular capillaries. It is an *outward pressure* from blood pressing on the fenestrated capillary walls. The glomerular capillary pressure forces fluid and solutes out of the blood into the Bowman capsule. This pressure is higher than that in

other capillaries of the body due to the smaller diameter of the efferent arteriole compared to that of the afferent arteriole and glomerular capillaries.

❷ **Capsular pressure.** The capsular pressure is an *inward pressure* that opposes filtration. Capsular pressure is due to pressure from the filtrate fluid in the capsular space.

❸ **Colloid osmotic pressure.** The colloid osmotic pressure is also an *inward pressure* that opposes filtration. It is due to the osmotic pressure of plasma proteins in the glomerular capillaries. Through osmosis, these proteins draw fluid back into the glomerular capillary from the Bowman capsule. The colloid osmotic pressure is greater at the end of the glomerular capillary than at its beginning because there is a higher protein concentration at the end of the glomerulus.

To calculate filtration pressure, all three filtration pressures are summed. In a normal kidney glomerular capillary pressure is greater than the combination of capsular pressure and colloid osmotic pressure. The filtration pressure is a net *outward* pressure (see figure 18.9):

Filtration pressure	=	Glomerular capillary pressure	–	Capsular pressure	– Colloid osmotic pressure
10 mm Hg	=	50 mm Hg	–	10 mm Hg	– 30 mm Hg

Regulation of Filtration

The blood pressure within the glomerular capillaries is fairly constant over a broad range of systemic blood pressure. Because the afferent and efferent arterioles can either dilate or constrict, the blood pressure is tightly regulated in the glomerular capillaries. Also, the concentration of blood proteins and the pressure inside the Bowman capsule are fairly constant. As a consequence, the filtration pressure and the rate of filtrate formation are usually maintained within a narrow range of values.

Understand **Apply It 1**

How would the filtration pressure change if the afferent arteriole is constricted? Would urine production tend to increase or decrease? Explain.

However, the filtration pressure does change dramatically under intense sympathetic stimulation. Because sympathetic neurons innervate the blood vessels of the kidney, sympathetic stimulation causes constriction of the kidney arteries. This constriction decreases renal blood flow and filtrate formation. Intense sympathetic stimulation, as occurs during **circulatory shock** or vigorous exercise, may significantly decrease filtrate formation and urine volume (see figure 18.17). One of the dangers of circulatory shock is that the renal blood flow can be so low that the kidneys suffer from lack of O2. If the O2 level remains too low for a long enough time, permanent kidney damage or complete kidney failure results. One important reason for treating circulatory shock quickly is to avoid damage to the kidneys. On the other hand, decreased sympathetic stimulation of renal blood arteries increases renal blood flow and increases urine volume (see figure 18.17). Higher systemic blood pressure inhibits the sympathetic output to the renal arteries.

Tubular Reabsorption

The process of tubular reabsorption entails nearly every type of cell transport mechanism you learned in chapter 3. **Tubular reabsorption** is the transport of water and solutes from the filtrate into the blood. Principally, water movement in the kidney is governed by osmosis. Recall that osmosis is the movement of water toward solutions with higher solute concentrations, or high osmotic pressure. Solute movement is quite often through diffusion across the renal tubule cells. Diffusion is the net movement of solutes down their concentration gradient. However, some molecules are too large to pass through the cell membrane, or the cell may need to move a molecule against its concentration gradient. In these instances, cells use transport proteins. There are several types of transport proteins used by renal tubule cells. For example, cotransport moves two molecules or ions in the same direction.

Proper tubular reabsorption is critical in preventing the body from becoming overly dehydrated and deficient in important materials. Nearly all (99%) of the water and solutes are rapidly returned to the blood via the renal tubules. The filtrate leaves the lumen of the Bowman capsule and flows first through the proximal convoluted tubule, into the loop of Henle, and the distal convoluted tubule and then finally into the collecting ducts. As the filtrate passes through these structures, many of the substances in

the filtrate are removed. Inorganic salts, organic molecules, and about 99% of the filtrate volume leave the renal tubule and enter the interstitial fluid. Because the pressure is low in the peritubular capillaries, these substances enter the peritubular capillaries and flow through the renal veins to enter the general circulation (see figure 18.8).

Reabsorption in the Proximal Convoluted Tubule

The proximal convoluted tubule is the site of the majority of reabsorption. The mechanisms underlying reabsorption can be better understood by considering the cells found there. The cells of the proximal convoluted tubule have numerous microvilli, which dramatically increase the surface area available for reabsorption. Figure 18.10 describes the process of reabsorption in the proximal convoluted tubule.

❶ Reabsorption of most solutes is linked to the diffusion of Na+ into the cells of the proximal convoluted tubule. There is a steep concentration gradient for Na+ from the filtrate into the cytoplasm of the cells of the proximal convoluted tubule. This concentration gradient is established by active transport of Na+ out of the cells of the proximal convoluted tubule. This movement of Na+ into these cells is responsible for the transport of many other solutes from the lumen of the proximal convoluted tubule into the cytoplasm of the tubule cells.

❷ Carrier molecules that transport amino acids, glucose, and other solutes are located within the proximal convoluted tubule cells. Each of these carrier molecules binds specifically to one of those substances to be transported and to Na+. The concentration gradient for Na+ provides the energy that moves both the Na+ and the other molecules or ions from the lumen into the tubule cell. Once the molecules are inside the cell, they enter the interstitial fluid by facilitated diffusion or cotransport. The number of carrier proteins limits the rate at which a substance can be transported.

❸ As solutes are transported out of the lumen, through the proximal convoluted tubule cells, and into the interstitial fluid, water follows by osmosis. By the time the filtrate has reached the end of the proximal convoluted tubule, its volume has been reduced by approximately 65%. However, because the proximal convoluted tubule is permeable to water, the concentration of the filtrate there remains about the same as that of the interstitial fluid (300 mOsm/L).

PROCESS Figure

PROCESS Figure 18.10 **Reabsorption in the Proximal Convoluted Tubule**

The proximal convoluted tubule is the primary location for reabsorption of solutes and water.

Understand **You learned that the epithelial cells of the proximal convoluted tubule have numerous microvilli. Why are the microvilli beneficial for the process of reabsorption?**

Apply

Apply It 2

People who suffer from untreated diabetes mellitus can experience very high levels of glucose in the blood. The glucose can easily cross the filtration membrane into the Bowman capsule. Normally, all the glucose is reabsorbed from the nephron. However, if the concentration of glucose in the nephron becomes too high, not all the glucose can be reabsorbed because the number of transport molecules in the cells of the proximal convoluted tubule is limited. How does the volume of urine produced by a person with untreated diabetes mellitus differ from that of a healthy person, and how does the concentration of the urine differ from that of a healthy person?

Reabsorption in the Loop of Henle

Earlier, we described the loop of Henle and its two limbs. The two limbs differ in the type of epithelial tissue present in each. This difference in cell type is linked to the permeability of each limb to water and solutes. Figure 18.11 describes reabsorption in each limb of the loop of Henle.

❶ *Reabsorption in the descending limb of the loop of Henle.* The epithelial tissue in the majority of the descending limb, in particular the thin segment, is simple squamous epithelial tissue (figure 18.11). Remember from chapter 4 that simple squamous cells are highly permeable to water, which means the descending limb is highly permeable to water. Water moves by osmosis out of the descending limb, while some solutes move by diffusion into the descending limb. By the time the filtrate has reached the end of the thin segment, the volume of the filtrate has been reduced by another 15% and its concentration has significantly increased to 1200 mOsm/L.

❷ *Reabsorption in the ascending limb of the loop of Henle.* As the loop of Henle makes its hairpin turn into the ascending limb, the simple squamous epithelium persists, but it has become impermeable to water (figure 18.11). However, it is still permeable to solutes, which exit the ascending limb, thereby again reducing the concentration of the filtrate.

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PROCESS Figure

PROCESS Figure 18.11 APR Reabsorption in the Loop of Henle: The Descending Limb and the Thin Segment of the Ascending Limb

The loop of Henle is a critical location for water reabsorption.

Apply **The desert kangaroo rat does not produce dilute, liquid urine, but instead produces thick, highly concentrated urine. Explain how having loops of Henle that are proportionally longer than those of other terrestrial animals allows for this. How is production of thick, concentrated urine advantageous to a desert animal?**

Figure 18.12 outlines the process of reabsorption in the thick segment of the ascending limb of the loop of Henle.

1. As the ascending limb continues, it is now called the thick segment. The thick segment of the ascending limb is impermeable to both water and solutes. Instead, the cells of the thick segment house multiple types of transport proteins including ATP-powered pumps and carrier molecules.
2. These carrier molecules remove a significant portion of the solutes from the filtrate, which then enters the interstitial fluid. It is this active transport of solutes that contributes to the kidneys' ability to conserve water. Cotransport is responsible for moving K^+ and Cl^- with Na^+ across the membrane of the ascending limb of the loop of Henle. Once inside the cells of the ascending limb, Cl^- and K^+ exit the cells of the ascending limb via facilitated diffusion.

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PROCESS Figure

PROCESS Figure 18.12 APR **Reabsorption in the Loop of Henle: The Thick Segment of the Ascending Limb**

The thick segment of the loop of Henle is not permeable to water.

What would happen to the concentration of solutes in the medulla if active transport of Na^+ in this segment of the loop of Henle were prevented?

As we follow the filtrate through the loop of Henle, we see that it becomes very concentrated toward the hairpin turn of the loop of Henle, but the concentration of the filtrate is reduced to about 100 mOsm/L by the time the fluid reaches the distal convoluted tubule.

Reabsorption in the Distal Convoluted Tubule and Collecting Duct

Some solutes (K^+ and H^+) are not reabsorbed until farther along the renal tubule in the distal convoluted tubule or collecting duct. The reabsorption of these solutes is generally under hormonal control and depends on the current conditions of the body. The distal convoluted tubule and the collecting duct are not always permeable to water; however, hormone regulation can change their permeability to water (see section 18.4). Reabsorption of water occurs through osmosis across the wall of the distal convoluted tubule and the collecting duct when the hormone ADH is present (see chapter 10).

The distal convoluted tubule also plays a major role in secretion, which is discussed later in this section.

Tubular Secretion

Tubular secretion is the movement of nonfiltered substances from the blood into the filtrate. These substances include toxic by-products of metabolism and drugs or molecules not normally produced by the body. As with tubular reabsorption, tubular secretion can be either active or passive. For example, ammonia is a toxic by-product of protein metabolism. It is produced when the epithelial cells of the renal tubule remove amine groups from amino acids, which diffuse into the lumen of the renal tubule. On the other hand, H^+, K^+, and penicillin, are actively secreted by either active transport or counter transport processes into the renal tubule. An example of an counter transport process in the kidney is the secretion of H^+, which plays a major role in regulating body fluid pH and is discussed in more detail in section 18.8.

Urine Concentration Mechanism

As you have just read, the kidneys are remarkable at regulating blood composition. The kidneys are able to produce very dilute or very concentrated urine while maintaining the extracellular fluid concentration very close to 300 mOsm/L. But how does the kidney move such a large volume of fluid from the blood into the filtrate and then back into the blood? The kidneys' ability to control the volume and concentration of the urine depends on three factors: (1) countercurrent mechanisms, (2) a medullary concentration gradient, and (3) hormonal mechanisms.

Countercurrent Mechanisms

The kidneys utilize a countercurrent mechanism. A countercurrent mechanism is one where fluid in separate structures flows in opposite directions relative to each other. As the fluids pass by each other, materials can be exchanged between the fluids.

The loop of Henle is responsible for a large percentage of a very high concentration of solutes that is found in the interstitial fluid within the medulla of the kidney. The permeability changes in the loop of Henle are responsible for its role in the countercurrent mechanism.

The vasa recta maintains the high solute concentration in the interstitial fluid. Because the flow rate and blood pressure in the vasa recta are so slow and very low, the blood and the interstitial fluid are always in equilibrium and solutes are not carried away from the interstitial fluid by the blood in the vasa recta.

Countercurrent Mechanisms: Medullary Concentration Gradient

The interstitial fluid in the medulla of the kidney has a very high solute concentration compared with that of the cortex. This is called the **medullary concentration gradient.** The high solute concentration of the interstitial fluid develops from (1) the actions of the countercurrent mechanisms and (2) the recycling of the protein breakdown product, urea. The concentration of solutes in the medulla increases from 300 mOsm/L to 1200 mOsm/L deep in the medulla at the tip of the renal pyramid (see figure 18.13).

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PROCESS Figure

PROCESS Figure 18.13 **Urine-Concentrating Mechanism**

The concentration gradient from the cortex to the inner medulla is shown on the left. Interstitial fluid increases in concentration from 300 mOsm/L in the cortex to 1200 mOsm/L in the medulla. The concentrations of the filtrate in different parts of the nephron are also shown.

What is the advantage of producing 180 L of filtrate each day only to reabsorb 178 L (99%) of the filtered material?

To create and maintain the medullary concentration gradient, the following processes occur:

1. *Countercurrent mechanism.* As filtrate travels through the descending limb of the loop of Henle, water moves across its simple squamous epithelium by osmosis toward the higher solute concentration in the interstitial fluid. Then, as the filtrate begins to move through the ascending limb, solutes diffuse out of the filtrate. This increases the concentration of the interstitial fluid even more. In addition, the cells of the thick segment of the ascending limb actively pump solutes into the interstitial fluid, causing a very concentrated solution to form.

   The vasa recta supply blood to the kidney medulla, and they remove excess water and solutes from the medulla without changing the high concentration

of solutes in the medullary interstitial fluid. The walls of the vasa recta are permeable to both water and solutes. As blood flows toward the medulla, water moves out of the vasa recta, and some solutes diffuse into them. As blood flows back toward the cortex, water moves into the vasa recta, and some solutes diffuse out of them (see figure 18.13). In addition, blood pressure in the vasa recta is very low and blood flow rate is extremely slow, even sluggish. This encourages ready diffusion of solutes into and back out of the vasa recta, ensuring the maintenance of the high medullary concentration gradient.

2. *Urea cycling.* Urea is responsible for a substantial part of the high solute concentration in the kidney medulla. Urea is recycled from the interstitial fluid through the renal tubules and back into the interstitial fluid.

   To summarize, several key events occur in the renal tubule to establish and maintain a high solute concentration:

   a. Sodium ions and other solutes are actively transported into the interstitial fluid of the medulla, maintaining a high solute concentration.

   b. Because in the vasa recta there is low blood pressure, and blood flows sluggishly, solutes are not washed away from the medulla.

   c. Much urea returns to the medulla from the collecting duct, rather than exiting with the urine.

Summary of Urine Formation

Following are the steps in urine production from the proximal convoluted tubule to the collecting duct (figure 18.13).

❶ In the average person, about 180 L of filtrate enter the proximal convoluted tubules daily.

❷ Glucose, amino acids, Na^+, Ca^{2+}, K^+, Cl^-, water, and other substances move from the lumens of the proximal convoluted tubules into the interstitial fluid. The excess solutes and water then enter the peritubular capillaries. Consequently, cells of the proximal convoluted tubule reabsorb approximately 65% of the filtrate, which moves solutes and water into the interstitial fluid.

❸ As the filtrate continues to flow through the renal tubule, it enters the descending limbs of the loops of Henle. As the descending limbs penetrate deep into the kidney medulla, the surrounding interstitial fluid has a progressively greater concentration. Water diffuses out of the loops of Henle as solutes slowly diffuse into them. By the time the filtrate reaches the deepest part of the loops of Henle, its volume has

been reduced by an additional 15% of the original volume, at least 80% of the filtrate volume has been reabsorbed, and its concentration has increased to about 1200 mOsm/L.

4. Both the thin and thick segments of the ascending limb of the loop of Henle are impermeable to water, but solutes diffuse out of the thin segment, and Na^+, Cl^-, and K^+ are symported from the filtrate into the interstitial fluid in the thick segments. The movement of solutes, but not water, across the wall of the ascending limbs causes the solute concentration of the filtrate to decrease from 1200 to about 100 mOsm/L by the time the filtrate again reaches the kidney cortex.
5. The volume of the filtrate does not change as it passes through the ascending limbs. As a result, the filtrate entering the distal convoluted tubules is dilute, compared with the concentration of the surrounding interstitial fluid.
6. The distal convoluted tubule and collecting duct are permeable to water when under hormonal regulation.
7. Around 1% or less of the filtrate remains as urine, when the body is conserving water.

The changes just described occur regardless of the concentration and volume of urine that the kidney finally produces. The mechanisms by which the kidney forms concentrated and dilute urine are described in section 18.4.

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18.4 REGULATION OF URINE CONCENTRATION AND VOLUME

Learning Outcome *After reading this section, you should be able to*

A. Explain how antidiuretic hormone, aldosterone, and atrial natriuretic hormone influence the volume and concentration of urine.

Given a solution in a container, such as a pan on a stove, it is possible to change its concentration by adding water to it or by boiling it, thereby removing water. Similarly, the kidneys change the concentration of the body fluids. For example, water reabsorption increases when body fluids become more concentrated, but water reabsorption decreases when body fluids become less concentrated. Therefore, the volume and composition of urine changes, depending on conditions in the body. When body fluid

concentration rises, the increased water reabsorption results in a small volume of concentrated urine. This eliminates solutes and conserves water, both of which help lower the body fluid concentration back to normal. On the other hand, when the body fluid concentration decreases, the decreased water reabsorption results in a large volume of dilute urine. As a result, water is lost, solutes are conserved, and the body fluid concentration increases.

The kidneys are also involved in the regulation of blood pressure. Urine production affects blood volume. An increase in blood volume causes blood pressure to rise, whereas a decrease in blood volume causes blood pressure to go down. In order to maintain blood pressure at its set-point, when blood volume increases above normal, the kidneys produce a large volume of urine. The loss of water in the urine lowers blood volume and blood pressure. For example, commonly used medications for lowering high blood pressure are diuretics, which cause a person to urinate more frequently. Conversely, if blood volume decreases below normal, the kidneys produce a small volume of urine, which increases blood volume and blood pressure.

Hormonal Mechanisms

Three major hormonal mechanisms are involved in regulating urine concentration and volume: (1) the renin-angiotensin-aldosterone mechanism, (2) the antidiuretic hormone (ADH) mechanism, and (3) the atrial natriuretic hormone (ANH) mechanism. Each mechanism is activated by different stimuli, but they work together to achieve homeostasis. Both the renin-angiotensin-aldosterone mechanism and the ANH mechanism are more sensitive to changes in blood pressure, whereas the ADH mechanism is more sensitive to changes in blood concentration.

Renin-Angiotensin-Aldosterone Mechanism

The renin-angiotensin-aldosterone mechanism is initiated under low blood pressure conditions. When blood pressure decreases, cells of the juxtaglomerular apparatuses in the kidneys secrete the enzyme **renin** (REE-nin). The kidneys detect the low blood pressure when juxtaglomerular cells detect reduced stretch of the afferent arteriole. Upon secretion, renin enters the blood and converts **angiotensinogen,** a plasma protein produced by the liver, to **angiotensin I. Angiotensin-converting enzyme (ACE)** is an enzyme produced by capillaries of organs such as the lungs. ACE converts angiotensin I to **angiotensin II**

(figure 18.14). Angiotensin II increases blood pressure and increases the sensation of thirst, and salt appetite. One stimulus that reduces renin secretion is when the blood pressure in the afferent arteriole is increased. In addition, angiotensin II stimulates the adrenal cortex to secrete aldosterone (see chapter 13). Aldosterone stimulates an increase in the reabsorption of Na^+ and Cl^- in the distal convoluted tubules and collecting ducts.

Figure 18.14 **Aldosterone and the Regulation of Na+ and Water in Extracellular Fluid**

Low blood pressure (BP) stimulates renin secretion from the kidney. Renin stimulates the production of angiotensin I, which is converted to angiotensin II, which in turn stimulates aldosterone secretion from the adrenal cortex. Aldosterone increases Na^+ and water reabsorption in the kidney.

Water follows the Na^+ and Cl^- from the filtrate into the blood. This reabsorption of water increases blood volume, which increases blood pressure back to its normal range (figure 18.14, see figure 18.17).

Understand

Apply It 3

Drugs that increase the urine volume are called diuretics. Some diuretics inhibit the active transport of Na^+ in the nephron. Explain how these diuretic drugs can cause an increase in urine volume.

Antidiuretic Hormone Mechanism

Antidiuretic (an-tee-die-you-RET-ik) **hormone (ADH)** is secreted by neurons in the posterior pituitary when the solute concentration of the blood or the interstitial fluid increases (see chapter 10). Even slight changes in the solute concentration will trigger ADH release. ADH promotes water conservation in the kidneys by increasing the permeability of the distal convoluted tubules and collecting ducts to water. This allows more water to be reabsorbed from the filtrate and the kidneys to produce a small volume of concentrated urine (figure 18.15; see figure 18.17). A low blood solute concentration inhibits ADH secretion, which reduces urine volume. This information may help you to answer this chapter's Learn to Apply It question.

Figure 18.15 **ADH and the Regulation of Extracellular Fluid Concentration**

(*a*) Increased blood solute concentration affects hypothalamic neurons, and decreased blood pressure affects baroreceptors. As a result of these stimuli, the posterior pituitary secretes ADH, which increases water reabsorption by the kidney. (*b*) ADH increases the permeability of the collecting duct to water by stimulating the insertion of water channel proteins, called aquaporins, into the membrane of the cells of the collecting duct.

ADH secretion is also regulated by changes in blood pressure. When baroreceptors that monitor blood pressure detect a significant decrease in

blood pressure, ADH secretion increases (figure 18.15; see figure 18.17). When baroreceptors detect a large increase in blood pressure, ADH secretion decreases. However, ADH is more sensitive to changes in blood osmolarity than to blood pressure.

Atrial Natriuretic Hormone

An increased blood pressure triggers the **atrial natriuretic** (ay-TREE-al nay-tree-yoo-RET-ik) **hormone (ANH)** mechanism. ANH is secreted from cardiac muscle cells in the right atrium of the heart when blood pressure in the right atrium increases above normal (figures 18.16 and 18.17). ANH acts on the kidney to decrease Na^+ reabsorption. Therefore, Na^+ remains in the tubules of the nephron. Water moves by osmosis into the tubules of the nephron toward the Na^+. This increases urine volume while reducing blood volume and blood pressure.

Figure 18.16 **ANH and the Regulation of Na+ and Water in Extracellular Fluid**

Increased blood pressure in the right atrium of the heart causes increased secretion of ANH, which increases Na^+ excretion and water loss in the form of urine.

Homeostasis Figure 18.17 **Hormonal Regulation of Blood Volume and Its Effect on Urine Volume and Concentration**

(1) Blood volume is in its normal range. (2) Blood volume increases outside the normal range, which causes homeostasis to be disturbed. (3) The control centers respond to the change in blood volume. (4) The control centers cause ADH and aldosterone secretion to decrease, which reduces water reabsorption. The control centers also cause dilation of renal arteries, which increases urine production. (5) These changes cause blood volume and thus blood pressure to decrease. (6) Blood volume returns to its normal range and homeostasis is restored. Observe the responses to a decrease in blood volume outside its normal range by following the *red arrows*.

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Apply It 4

René worked as a nurse in a hospital. Because she was very observant, she recognized that one of her patients had received a much larger volume of an intravenous (IV) saline solution than had been ordered. A saline solution consists of NaCl but also contains other solutes, such as small amounts of KCl. Saline solutions have the same concentration as body fluids. Explain the effect of the large volume of IV saline solution on the patient's rate of urine production, and describe the role of ADH, ANH, and aldosterone in controlling the change in urine production.

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18.5 URINE MOVEMENT

Learning Outcomes *After reading this section, you should be able to*

A. Describe the ureters, urinary bladder, and urethra.
B. Describe the micturition reflex

Anatomy and Histology of the Ureters, Urinary Bladder, and Urethra

The **ureters** are small tubes that carry urine from the renal pelvis of the kidney to the posterior inferior portion of the urinary bladder (figure 18.18). The **urinary bladder** is a hollow, muscular container that lies in the pelvic cavity just posterior to the pubic symphysis. It stores urine; thus, its size depends on the quantity of urine present. The urinary bladder can hold from a few milliliters (mL) to a maximum of about 1000 mL of urine. When the urinary bladder reaches a volume of a few hundred mL, its wall is stretched enough to activate a reflex that causes the smooth muscle of the urinary bladder to contract, and most of the urine flows out of the urinary bladder through the urethra. Cystitis (sis-TI-tis) is an

inflammation of the urinary bladder, which usually results from a bacterial infection. Typically, bacteria from outside the body enter the bladder. Infection by the bacterium E. coli is the most common cause of cystitis.

Figure 18.18 APR **Ureters and Urinary Bladder**

(*a*) Ureters extend from the renal pelvis to the urinary bladder. (*b*) The walls of the ureters and the urinary bladder are lined with transitional epithelium, which is surrounded by a connective tissue layer (lamina propria), smooth muscle layers, and a fibrous adventitia. (*c*) Section through the wall of the urinary bladder.

(photo): ©Victor Eroschenko

The **urethra** is the tube that carries urine from the urinary bladder to the outside of the body. The triangle-shaped portion of the urinary bladder located between the opening of the ureters and the opening of the urethra is called the **trigone** (TRY-gohn; triangle). This region is unique and does not expand with the urinary bladder wall as it fills. This causes the trigone to act as a funnel for emptying the urinary bladder.

Transitional epithelium lines both the ureters and the urinary bladder. Transitional epithelium is specialized, so that the cells slide past one another, and the number of cell layers decreases as the volume of the ureters and urinary bladder increases (see chapter 4). As the volume of the urinary bladder decreases, transitional epithelial cells assume their former shape and form a greater number of cell layers.

MICROBES IN YOUR BODY

Can Bacteria Actually Help Cure Urinary Bladder Cancer?

In the United States, there are more than 60,000 new cases of urinary bladder cancer diagnosed each year; it is the ninth leading type of cancer. However, if the cancer is detected and treated before it penetrates the urinary bladder's muscular wall or spreads to other areas of the body, the 5-year survival rate is 77%. Reliable treatments can resolve these cases relatively quickly. Surprisingly, the most common treatment for early-stage bladder cancer tumors is the introduction of a fluid containing live tuberculosis-causing bacteria into the bladder.

At least 50% of urinary bladder cancer cases can be attributed to cigarette smoking, even 10 years or more after a person has quit smoking.

In about 80–90% of urinary bladder cancer cases, the first sign is blood in the urine, called macrohematuria. Confirmation is usually done with a procedure called **cystoscopy** (si-STOS-kuh-pee), in which a catheter is inserted into the bladder to view the wall and collect cells, which are then examined under a microscope to look for abnormalities in appearance.

The treatments for urinary bladder cancer are dependent on how deeply the tumor has penetrated into the bladder wall. In earlier stages, treatment is more effective. If the tumor is quite small and shallow in the endothelium, the cancerous cells are scraped off the bladder wall. In other cases, in which the tumor is superficial but somewhat more advanced than the earliest stage, immunotherapy with intravesicular (inside the bladder) delivery of a medicine known as Bacillus Calmette-Guérin (BCG) is used. BCG is a live, attenuated (weakened) strain of *Myocobacterium bovis,* the bacterium that causes tuberculosis in cattle, but it can infect other organisms, including humans. Because the BCG fluid is isolated within the bladder, other organs in the body are not usually exposed to the bacteria.

The cancer cells are infected by the bacteria, induces destruction of the infected cells by the immune system (see chapter 14). The average treatment time is about 6 weeks. The BCG urinary bladder cancer treatment is an elegant example of how knowledge of body systems can be applied in an unexpected way: purposefully infecting a patient with bacteria so cancer cells are destroyed by the patient's immune system.

Layers of smooth muscle and connective tissue compose the walls of the ureter and urinary bladder. Regular waves of smooth muscle contraction in the ureters produce the force that causes urine to flow from the kidneys to the urinary bladder. Contractions of smooth muscle in the urinary bladder force urine to flow from the bladder through the urethra.

At the junction of the urinary bladder and the urethra, smooth muscle forms an **internal urethral sphincter** that prevents urine leakage from

the urinary bladder. In males, the internal urethral sphincter contracts to keep semen from entering the urinary bladder during sexual intercourse (see chapter 19). The specific anatomy and physiology of the internal urethral sphincter is more clearly detailed for the male urethra. For the female urethra, the details are not as well established. Females clearly have smooth muscle fibers within the wall of the urethra at the neck of the bladder. These smooth muscle fibers assist with preventing urine leakage, but whether these fibers form a distinct sphincter is still under scrutiny. Both males and females have a well-defined **external urethral sphincter.** The external urethral sphincter is formed of skeletal muscle that surrounds the urethra as the urethra extends through the pelvic floor. The external urethral sphincter allows a person to voluntarily start or stop the flow of urine through the urethra.

In males, the urethra extends to the end of the penis, where it opens to the outside. The female urethra is much shorter (approximately 4 cm) than the male urethra (approximately 20 cm) and opens into the vestibule anterior to the vaginal opening.

Understand ***Apply It 5***

Are males or females more prone to cystitis? Explain.

Control of the Micturition Reflex by Higher Brain Centers

Figure 18.19 illustrates the control of the micturition reflex by higher brain centers.

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PROCESS Figure

PROCESS Figure 18.19 APR Micturition Reflex

The micturition reflex is under parasympathetic regulation.

How might the urinary bladder be affected by damage to spinal cord nerves in the sacrum?

A Voluntary initiation of micturition requires an increase in action potentials sent from the cerebrum to facilitate the micturition reflex and to voluntarily relax the external urethral sphincter. In addition, voluntary contraction of the abdominal muscles increases abdominal pressure and thereby enhances the micturition reflex by increasing the pressure applied to the urinary bladder wall. Awareness of the need to urinate occurs because stretch of the urinary bladder stimulates sensory nerve fibers that increase action potentials carried to the brain by ascending tracts in the spinal cord. Irritation of the urinary bladder or the urethra by a bacterial infection or some other condition can also initiate the urge to urinate, even though the urinary bladder is nearly empty.

B Because of the micturition reflex, action potentials conducted along somatic motor nerves to the external urethral sphincter decrease, which causes the sphincter to relax. The micturition reflex is an automatic reflex, but it can be inhibited or stimulated by higher centers in the brain. The higher brain centers prevent micturition by sending action potentials through the spinal cord to decrease the intensity of the autonomic reflex that stimulates urinary bladder contractions and to stimulate nerve fibers that keep the external urethral sphincter contracted. The ability to voluntarily inhibit micturition develops at the age of 2–3 years.

A kidney stone, or renal calculus, can cause excruciating and debilitating discomfort in the lateral abdominal region, which can radiate to the inguinal region on the left side of the body. Peristaltic contractions of the ureter force irregularly shaped kidney stones through the narrow ureter, which causes inflammation and pain. The majority of kidney stones consist mainly of calcium oxylate. Increasing fluid intake such that the kidneys produce at least 2 liters of urine each day helps prevent kidney stones from forming. Keeping the urine dilute reduces the likelihood of calcium salts precipitating and forming additional kidney stones. A common treatment for kidney stones is **lithotripsy** (LITH-oh-trip-see), an ultrasound technique that pulverizes kidney stones into small particles that can pass easily through the ureter.

Micturition

Micturition Reflex

Figure 18.19 also illustrates the steps in the micturition reflex.

❶ The **micturition** (mik-choo-RISH-un) **reflex** is activated by stretch of the urinary bladder wall. As the urinary bladder fills with urine, pressure increases, stimulating stretch receptors in the wall of the urinary bladder.

❷ Action potentials produced by stretch receptors are carried along pelvic nerves to the sacral region of the spinal cord. Integration of the reflex occurs in the spinal cord, and action potentials are conducted along parasympathetic nerve fibers to the urinary bladder. Parasympathetic action potentials cause the urinary bladder to contract.

❸ Action potentials are carried by parasympathetic nerves to contract the smooth muscles of the urinary bladder. The external urethral sphincter is normally contracted as a result of stimulation from the somatic motor nervous system. Decreased action potentials carried by somatic motor nerves cause the external urethral sphincter to relax.

18.6 BODY FLUID COMPARTMENTS

Learning Outcome *After reading this section, you should be able to*

A. List the major body fluid compartments.

Approximately 60% of the total body weight of an adult male consists of water. Approximately 50% of the total body weight of an adult female is water. Because the water content of adipose tissue is relatively low, the fraction of the body's weight composed of water decreases as the amount of adipose tissue increases. A smaller percentage of the body weight of an adult female consists of water because females generally have a greater percentage of body fat than do males. Water and the ions dissolved in it are distributed in two major compartments: (1) the intracellular fluid compartment and (2) the extracellular fluid compartment (table 18.2). Water and ions move between these compartments, but their movement is regulated.

TABLE 18.2 Approximate Volumes of Body Fluid Compartments*

Age of Person	Total Body Water	Intracellular Fluid	Plasma	Extracellular Fluid Interstitial	Total
Infant	75	45	4	26	30
Adult male	60	40	5	15	20
Adult female	50	35	5	10	15
*Expressed as percentages of body weight.					

The **intracellular fluid compartment** consists of all of the fluid inside the cells of the body. This fluid is part of the cytoplasm of the cell, and it has a similar composition in all the cells of the body. The intracellular fluid compartment accounts for the majority of the water in the body, or about 70%. This equals approximately 40% of the body's total weight.

The **extracellular fluid compartment** accounts for around 30% of all the water in the body, which is equal to about 20% of the body's total weight. This fluid consists of the fluid outside all the cells of the body. The extracellular fluid is distributed throughout the body and is divided into multiple subcompartments, including: (1) interstitial fluid between cells, (2) plasma of the blood, (3) lymph within lymphatic vessels, (4) cerebrospinal fluid of the brain and spinal cord, and (5) synovial fluid within synovial joints. However, the interstitial fluid and plasma constitute the vast majority of the extracellular fluid. The **interstitial** (in-ter-STISH-al) **fluid** is the fluid found surrounding the cells of the body and filling the extracellular spaces. **Plasma** (PLAZ-mah) is the liquid portion of the blood inside all the blood vessels in the body.

Composition of the Fluid in the Body Fluid Compartments

Intracellular fluid has a similar composition from cell to cell. It contains a relatively high concentration of ions, such as K+, magnesium (Mg^2+), phosphate (PO_4^{3-}), and sulfate (SO_4^{2-}), compared to the extracellular fluid. It has a lower concentration of Na^+, Ca^{2+}, Cl^-, and HCO_3^- than does the extracellular fluid. The concentration of protein in the intracellular fluid is also greater than that in the extracellular fluid. Like intracellular fluid, the extracellular fluid has a fairly consistent composition from one area of the body to another.

Exchange Between Body Fluid Compartments

The cell membranes that separate the body fluid compartments are selectively permeable. Water continually passes through them, but ions dissolved in the water do not readily pass through the cell membrane. Water movement is regulated mainly by hydrostatic pressure differences and osmotic differences between the compartments. For example, water moves across the wall of the capillary at the arterial end of the capillary because the blood pressure there is great enough to force fluid into the interstitial space. At the venous end of the capillary, the blood pressure is much lower, and fluid returns to the capillary because the osmotic pressure is higher inside the capillary than outside it (see chapter 13).

Despite specific ion differences, under normal conditions, the total osmotic pressure in each compartment is approximately equal. This allows for a continuous, extensive exchange of water and electrolytes between the compartments (figure 18.20*a*). If the composition of one compartment changes a great deal, water movement will shift toward the compartment with the higher solute concentration. Thus, one of the greatest influences on the maintenance of homeostatic fluid balance between fluid compartments is osmosis. Osmosis is the diffusion of water toward a solution with a higher solute concentration. For example, during an inflammatory response to an infection, the permeability of the capillary wall increases. The increased permeability allows proteins to exit the plasma and enter the interstitial fluid. Water will then move by osmosis out of the plasma and into the interstitial fluid, which results in swelling, or edema (figure 18.20*b*). On the other hand, if the blood solute concentration becomes greater than that of the interstitial fluid, water will move by osmosis into the plasma. This type of response is seen when a person becomes dehydrated (figure 18.20*c*).

Figure 18.20 **Influence of Osmotic Pressure on Fluid Movement**
(*a*) When osmotic pressures on each side of a cell membrane are equal, there is no net movement of water molecules. (*b*) If osmotic pressure is higher in the interstitial fluid than that in the blood, there is a net movement of water by osmosis out of the blood. (*c*) If osmotic pressure of the blood is higher than that of the interstitial fluid, there is net movement of water by osmosis into the blood.

18.7 REGULATION OF EXTRACELLULAR FLUID COMPOSITION

Learning Outcome ***After reading this section, you should be able to***

A. Describe the mechanisms by which Na^+, K^+, and Ca^{2+} are regulated in the extracellular fluid.

Homeostasis requires that the intake of substances equals their elimination. Needed water and ions enter the body by ingestion; excess water and ions exit the body by excretion. The amounts of water and ions entering and leaving the body can vary over the short term. For example, greater quantities of water and ions are lost in the form of perspiration on warm days than on cool days, and varying amounts of water and ions may be lost in the form of feces. However, over a long period, the total amount of water and ions in the body does not change unless the individual is growing, gaining weight, or losing weight. Regulating the amounts of water and ions in the body involves the coordinated participation of several organ systems, but the kidneys are the most important, with the skin, liver, and digestive tract playing supporting roles. Two mechanisms help regulate the levels of ions in the extracellular fluid: (1) thirst regulation and (2) ion concentration regulation.

Thirst Regulation

Water intake is controlled by neurons in the hypothalamus, collectively called the **thirst center.** Thirst is the sensation that induces an urge to drink liquids. An increase in thirst is usually associated with a reduction in the water content of the body, whereas a decrease in thirst is associated with adequate water content of the body (figure 18.21). Drinking a dilute solution decreases the blood solute concentration. This decreases the sensation of thirst. A sudden drop in blood pressure, such as during shock, activates the thirst center, triggering the sensation of thirst. Consumption of water increases the blood volume and allows the blood pressure to return to its normal value. Other stimuli can also trigger the sensation of thirst. For example, if the mucosa of the mouth becomes dry, the thirst center is activated. Thirst is one of the important means of regulating extracellular fluid volume and concentration.

Figure 18.21 **Thirst and the Regulation of Extracellular Fluid Concentration**

Increased blood concentration affects hypothalamic neurons, and large decreases in blood pressure affect baroreceptors in the aortic arch, carotid sinuses, and right atrium. These stimuli cause an increase in thirst, which increases water intake. Increased water intake reduces blood concentration and increases blood volume.

Ion Concentration Regulation

If the water content or concentration of ions in the extracellular fluid deviates from its normal range, cells cannot control the movement of substances across their cell membranes or the composition of their intracellular fluid. The consequence is abnormal cell function or even cell death. Keeping the extracellular fluid composition within a normal range is therefore required to sustain life.

Regulating the concentrations of positively charged ions, such as Na^+, K^+, and Ca^{2+}, in the body fluids is particularly important. Action potentials, muscle contraction, and normal cell membrane permeability depend on the maintenance of a narrow range of concentrations for these ions. Important mechanisms control the concentrations of these ions in the body. Negatively charged ions, such as Cl^-, are secondarily regulated by the mechanisms that control the positively charged ions. The negatively charged ions are attracted to the positively charged ions; when the positively charged ions are transported, the negatively charged ions move with them.

Sodium Ions

Sodium ions (Na^+) are the dominant ions in the extracellular fluid. Osmotic pressure is the force that causes the net movement of water molecules toward an area with a higher solute concentration. Solutions with a higher solute concentration have a greater osmotic pressure than solutions with a lower solute concentration. About 90–95% of the osmotic pressure of the extracellular fluid results from Na^+ and from the negative ions associated with them.

The recommended intake of Na^+ is 2.4 grams per day (g/day), because of its association with high blood pressure in some people. Most people in the United States consume two to three times the recommended amount of Na^+. The kidneys provide the major route by which the excess Na^+ is excreted.

Sodium ions are also excreted from the body in perspiration, or **sweat.** Normally, only a small quantity of Na^+ is lost each day in the form of sweat, but the amount increases during heavy exercise in a warm environment.

The primary mechanisms that regulate Na^+ concentrations in the extracellular fluid are sensitive to changes in extracellular fluid concentration or blood pressure (see figure 18.17). These mechanisms do not directly monitor Na^+ levels. The quantity of Na^+ in the body has a dramatic effect on extracellular osmotic pressure and extracellular fluid volume. For example, if the quantity of Na^+ in the extracellular fluid increases, its concentration also increases. This promotes ADH secretion. ADH stimulates both water reabsorption in the kidneys and thirst. Overall, ADH is a water conservation hormone. A decrease in the quantity of Na^+ in the body causes an opposite set of responses. ADH secretion decreases, which allows a large volume of dilute urine to be produced and decreases the sensation of thirst. As a result of these changes, extracellular

concentration increases. By regulating extracellular fluid concentration and extracellular fluid volume, the concentration of Na^+ in the body fluids is maintained within a narrow range of values.

Elevated blood pressure under resting conditions increases Na^+ and water excretion. If blood pressure is low, the total Na^+ content of the body is usually also low. In response to low blood pressure, mechanisms such as the renin-angiotensin-aldosterone mechanism are activated, increasing Na^+ concentration and water volume in the extracellular fluid.

When blood pressure is increased, the walls of the heart, particularly in the right atrium, are stretched. The increased stretch causes specialized cells in the right atrium to secrete the hormone ANH. ANH acts on the kidneys to increase urine production by inhibiting the reabsorption of Na^+. It also inhibits the effect of ADH on the distal convoluted tubules and collecting ducts and inhibits ADH secretion.

Potassium Ions

Electrically excitable tissues, such as muscles and nerves, are highly sensitive to slight changes in the extracellular K^+ concentration. The extracellular concentration of K^+ must be maintained within a narrow range for these tissues to function normally.

Aldosterone plays a major role in regulating the concentration of K^+ in the extracellular fluid. Dehydration, circulatory system shock resulting from plasma loss, and tissue damage due to injuries such as severe burns all cause extracellular K^+ concentrations to increase above normal. In response, aldosterone secretion from the adrenal cortex increases and causes K^+ secretion to increase.

A low K^+ concentration in the extracellular fluid slows aldosterone secretion from the adrenal cortex. Without aldosterone, the kidneys secrete less K^+.

Calcium Ions

The extracellular concentration of Ca^{2+}, like that of other ions, is maintained within a narrow range. Changes in the extracellular concentration of Ca^{2+} have dramatic effects on the electrical properties of excitable tissues. For example, decreased extracellular Ca^{2+} concentrations make cell membranes more permeable to Na^+, thus making them more electrically excitable. Decreased extracellular concentrations of Ca^{2+} cause spontaneous action potentials in nerve and muscle cells, resulting in hyperexcitability and muscle tetany. Increased extracellular Ca^{2+}

concentrations make cell membranes less permeable to Na^+, thus making them less electrically excitable. Increased extracellular concentrations of Ca^{2+} inhibit action potentials in nerve and muscle cells, resulting in reduced excitability and either muscle weakness or paralysis.

There are three major hormones that regulate blood levels of Ca^{2+}: (1) parathyroid hormone, (2) vitamin D^3, and (3) calcitonin (see figure 10.17).

Parathyroid hormone (PTH) is secreted by the parathyroid glands when blood Ca^{2+} levels are too low. PTH increases blood Ca^{2+} through three principal means:

1. *Osteoclasts.* PTH stimulates osteoclasts to reabsorb bone, which increases blood levels of Ca^{2+} and phosphate (see chapter 6).
2. *Renal tubules.* PTH increases Ca^{2+} reabsorption from the kidney tubules. However, PTH stimulates phosphate excretion in the kidneys, which results in low blood levels of phosphate.
3. *Vitamin D_3.* PTH increases the rate of active vitamin D^3 formation, which indirectly increases Ca^{2+} levels through the actions of vitamin D_3.

Lack of PTH secretion causes a rapid reduction in blood Ca^{2+} levels. This could result in death, primarily due to constant contraction of the respiratory muscles. Vitamin D can be obtained from the diet or from vitamin D_3 synthesis. Normally, vitamin D_3 synthesis is adequate; however, because ultraviolet light is required for this process, prolonged lack of sun exposure reduces vitamin D_3 blood levels. Without vitamin D_3, the transport of Ca^{2+} across the wall of the digestive tract is very low. This leads to inadequate Ca^{2+} absorption, even though the person may be consuming a large amount of this ion. Thus, Ca^{2+} absorption depends on getting adequate amounts of calcium and vitamin D.

Calcitonin (kal-sih-TONE-in) is secreted by the parafollicular cells of the thyroid gland. Calcitonin lowers extracellular Ca^{2+} levels. However, greater-than-normal calcitonin levels in the blood do not reduce blood levels of Ca^{2+} to below-normal values. The major effect of calcitonin is in bone, where it inhibits osteoclasts. Thus, calcitonin prevents bone

degradation, which keeps blood Ca^{2+} levels from rising (see chapter 6). However, PTH is more important than calcitonin for blood Ca^{2+} regulation.

Phosphate and Sulfate Ions

Some ions, such as **phosphate ions** (PO_4^{3-}) and **sulfate ions** (SO_4^{2-}), are reabsorbed by active transport in the kidneys. The rate of reabsorption is slow, so that if the concentration of these ions in the filtrate exceeds the nephron's ability to reabsorb them, the excess is excreted into the urine. As long as the concentration of these ions is low, nearly all of them are reabsorbed by active transport. This mechanism plays a major role in regulating the concentration of PO_4^{3-} and SO_4^{2-} in the body fluids.

18.8 REGULATION OF ACID-BASE BALANCE

Learning Outcome ***After reading this section, you should be able to***

A. Illustrate how the mechanisms that regulate the body fluid pH function, by explaining how they respond to decreasing and increasing pH in the body fluids.

The concentration of H^+ in the body fluids is reported as the pH. The body fluid pH is maintained between 7.35 and 7.45; any deviation from that range is life-threatening. The mechanisms that regulate body fluid pH are critical for survival. The pH of body fluids is controlled by three factors: (1) buffer systems (2) the respiratory system, and (3) the kidneys. When the pH of body fluids is not properly maintained, the result is acidosis or alkalosis.

Regulation of Acid-Base Balance by Buffer Systems

Buffers are chemicals that resist a change in the pH of a solution when either acids or bases are added to the solution (see chapter 2). The buffers in the body fluids contain salts of either weak acids or weak bases that bind to H^+ when H^+ increases in those fluids, or release H^+ when H^+ decreases in those fluids. Buffers tend to keep the H^+ concentration, and thus the pH, within a narrow range of values (figure 18.22) because of these characteristics. The three major buffers in the body fluids are (1) the protein buffer system, (2) the PO_4^{3-} buffer system, and (3) the HCO_3^- buffer system.

Homeostasis Figure 18.22 **Summary of the Regulation of Acid-Base Balance**

(1) Blood pH is in its normal range. (2) Blood pH increases outside the normal range, which causes homeostasis to be disturbed. (3) The blood pH control centers respond to the change in blood pH. (4) The control centers cause decreased H^+ secretion from the blood and increased carbonic acid production, which increases blood H^+ concentration. (5) These changes cause blood pH to decrease. (6) Blood pH returns to its normal range, and homeostasis is restored. Observe the responses to a decrease in blood pH outside its normal range by following the lower *red arrows*.

Proteins and PO_4^{3-} in the body fluids bind reversibly to H^+. The binding of excess H^+ to proteins and PO_4^{3-} prevents a decrease in pH. Conversely, when the H^+ concentration decreases, proteins and PO_4^{3-} release H^+, which prevents an increase in pH.

Monohydrogen phosphate ions (HPO_4^{2-}) bind to H^+ to form dihydrogen phosphate ions (H_2PO^{4-}) when excess H^+ is present. When H^+ concentration declines, some of the H^+ separate from the $H_2PO_4^-$.

Proteins are able to function as buffers because their amino acids have side chains that function as weak acids and weak bases. Many side chains contain carboxyl groups (–COOH) or amine groups ($-NH_2$).

The bicarbonate (HCO_3^-) buffer system is unable to bind as many hydrogen ions as can proteins and PO_4^{3-} buffers, but the HCO_3^- buffer system is critical because it can be regulated by the respiratory and urinary systems. Carbon dioxide (CO_2) binds to water (H_2O) to form carbonic acid (H_2CO_3), which in turn forms H^+ and HCO_3^- as follows:

$$\underset{\text{Carbon dioxide}}{CO_2} + \underset{\text{Water}}{H_2O} \overset{\text{Carbonic anhydrase}}{\rightleftarrows} \underset{\text{Carbonic acid}}{H_2CO_3} \rightleftarrows \underset{\text{Hydrogen ion}}{H^+} + \underset{\text{Bicarbonate ion}}{HCO_3^-}$$

The reaction between CO_2 and H_2O is catalyzed by an enzyme, called carbonic anhydrase, which is found in red blood cells and on the surface of capillary epithelial cells (see chapter 15). The enzyme accelerates the rate at which the reaction proceeds in either direction.

The higher the concentration of CO_2, the lower the pH becomes. This is because a greater amount of H_2CO_3 is formed, which forms a greater amount of H^+ and HCO_3^-. An increase in H^+ concentration lowers the pH. However, the reaction is reversible. If CO_2 levels decline, the equilibrium shifts in the opposite direction. That is, H^+ and HCO_3^- combine to form H_2CO_3, which then forms CO_2 and H_2O, and the pH increases.

Regulation of Acid-Base Balance by the Respiratory System

The **respiratory system** responds rapidly to a change in pH and helps bring the pH of body fluids back toward normal. Neurons in the respiratory center of the brain are sensitive to CO_2 levels and acidic pH. High CO_2 levels and low pH cause an elevated rate and depth of respiration. As a result, CO_2 is eliminated from the body through the lungs at a greater rate, and the concentration of CO_2 in the body fluids decreases. As CO_2 levels decline, the concentration of H^+ also declines. The pH therefore rises back toward its normal range (figure 18.22).

Understand **Apply It 6**

Under stressful conditions, some people hyperventilate. What effect will a rapid rate of ventilation have on the pH of body fluids? In addition, why might a person who is hyperventilating benefit from breathing into a paper bag? (Hint: this question applies to regulation of acid-base balance by the respiratory system).

Low blood CO_2 levels or increased body fluid pH reduces the rate and depth of respiration. As a consequence, the rate at which CO_2 is eliminated from the body is reduced. Carbon dioxide then accumulates in the body fluids because it is continually produced as a by-product of metabolism. As CO_2 accumulates in the body fluids, so does H^+, resulting in a decreased pH.

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Regulation of Acid-Base Balance by the Kidneys

The nephrons of the kidneys secrete H^+ into the urine and therefore can directly regulate the pH of the body fluids. The kidney is a powerful regulator of pH, but it responds more slowly than does the respiratory system. Cells in the walls of the distal convoluted tubule are primarily responsible for the secretion of H^+. When blood pH is too low, secretion of H^+ in the distal convoluted tubules increases (figure 18.22). At the same time, reabsorption of HCO_3^- increases. The increased rate of H^+ secretion and the increased rate of HCO_3^- reabsorption both cause the blood pH to rise toward its normal value. On the other hand, when blood pH is too high, secretion of H^+ in the distal convoluted tubules decreases. In addition, the amount of HCO_3^- lost in the urine increases. The decreased

rate of H^+ secretion and the increased rate of HCO_3^- secretion both cause the blood pH to decrease toward its normal value.

Acidosis and Alkalosis

Failure of the buffer systems, the respiratory system, or the urinary system to maintain normal pH levels can result in acidosis or alkalosis.

Acidosis

Acidosis (ass-ih-DOH-sis) occurs when the blood pH falls below 7.35. The central nervous system malfunctions, and the individual becomes disoriented and, as the condition worsens, may become comatose. Acidosis is separated into two categories. **Respiratory acidosis** results when the respiratory system is unable to eliminate adequate amounts of CO_2 from the blood. Carbon dioxide accumulates in the blood, causing the pH of the body fluids to decline. **Metabolic acidosis** results from excess production of acidic substances, such as lactic acid and ketone bodies, because of increased metabolism or decreased ability of the kidneys to eliminate H^+ in the urine.

Apply It 7

Adam suffers from severe emphysema. Gas exchange in his lungs is not adequate, and he requires supplementary O_2. But even though his blood CO_2 levels are elevated, his blood pH is close to normal. Explain. (Hint: this question applies to regulation of acid-base balance by the kidneys)

Alkalosis

Alkalosis (al-kah-LO-sis) occurs when the blood pH increases above 7.45. A major effect of alkalosis is hyperexcitability of the nervous system. Peripheral nerves are affected first, resulting in spontaneous nervous stimulation of muscles. Spasms and tetanic contractions result, as can extreme nervousness or convulsions. Tetany of respiratory muscles can cause death. **Respiratory alkalosis** results from hyperventilation, as can occur in response to stress. **Metabolic alkalosis** usually results from the rapid elimination of H^+ from the body, as occurs during severe vomiting or when excess aldosterone is secreted by the adrenal cortex.

Acute Renal Failure

Background Information

A large piece of machinery overturned at a construction site, trapping Roger for several hours. Roger's blood pressure decreased to very low levels due to blood loss, edema in the inflamed tissues, and emotional shock. Twenty-four hours after the accident, Roger's urine volume began to decrease. His urinary Na^+ concentration increased, but his urine concentration decreased. Cellular debris was evident in his urine.

For approximately 7 days, Roger required renal dialysis to maintain his blood volume and ion concentrations within normal ranges. In Roger's case, acute renal failure was caused by prolonged low blood pressure and lack of blood flow to the kidneys. The reduced blood flow caused damage to the epithelial lining of the kidney tubules. The period of reduced urine volume resulted from tubular damage. Dead and damaged tubular cells sloughed off into the tubules and blocked them, so that filtrate could not flow through. In addition, the filtrate leaked from the blocked or partially blocked tubules back into the interstitial spaces and therefore back into the blood. As a result, the amount of filtrate that became urine was markedly reduced.

Blood levels of urea and of creatine usually increase due to reduced filtrate formation and reduced function of the tubular epithelium. A small amount of urine is produced that has a high Na^+ concentration, although the concentration is usually close to the concentration of the body fluids. The kidney is not able to reabsorb Na^+, nor can it effectively concentrate urine. Figure 18.23 illustrates the far-reaching effects of acute renal failure on other systems of the body.

Figure 18.23 Acute Renal Failure

Acute renal failure has significant effects on other organ systems in the body, as this diagram illustrates.

Treatments for Renal Failure

Hemodialysis (HEE-moh-dye-AL-ih-sis) is a substitute for the excretory functions of the kidney. Hemodialysis is based on blood flow through tubes composed of a selectively permeable membrane. Blood is usually taken from an artery, passed through the tubes of the dialysis machine, and then returned to a vein (figure 18.24). On the outside of the dialysis tubes is a fluid, called dialysis fluid, which contains the same concentration of solutes as normal plasma, except for the metabolic waste products. As a consequence, the metabolic wastes diffuse from the blood to the dialysis fluid. The dialysis membrane has pores that are too small to allow plasma proteins to pass through them, and because the dialysis fluid contains the same beneficial solutes as the plasma, the net movement of these substances is zero.

Figure 18.24 Hemodialysis

During hemodialysis, blood flows through a system of tubes composed of a selectively permeable membrane. Dialysis fluid, which has a composition similar to that of normal blood (except that the concentration of waste products is very low), flows in the opposite direction on the outside of the dialysis tubes. Waste products, such as urea, diffuse from the blood into the dialysis fluid. Other substances, such as Na^+, K^+, and glucose, can diffuse from the blood into the dialysis fluid if they are present in higher than normal concentrations, because these substances are present in the dialysis fluid at the same concentrations found in normal blood.

Peritoneal (per-ih-toh-NEE-al) **dialysis** is an alternative to hemodialysis. The principles by which peritoneal dialysis works are the same as for hemodialysis, but the dialysis fluid flows through a tube inserted into the peritoneal cavity. The visceral and parietal peritonea act as the dialysis membrane. Waste products diffuse from the blood vessels beneath the peritoneum, across the peritoneum, and into the dialysis fluid.

Kidney transplants are sometimes performed on people who have severe renal failure. The major cause of kidney transplant failure is rejection by the recipient's immune system. Physicians therefore attempt to match the immune characteristics of the donor and recipient to reduce the tendency for rejection. Even with careful matching, recipients have to take medication for the rest of their lives to suppress their immune reactions. But in most cases, the transplanted kidney functions well.

Apply It 8

Nine days after the accident, Roger began to appear pale, became dizzy on standing, and was very weak and lethargic. His hematocrit was elevated, and his heart was arrhythmic. Explain these manifestations.

TABLE 18.3 REPRESENTATIVE DISEASES AND DISORDERS: Urinary System	
Condition	**Description**

Condition	Description
Inflammation of the Kidneys	
Glomerulonephritis (gloh-MER-you-loh-nef-RYE-tis)	Inflammation of the filtration membrane within the renal corpuscle, causing increased membrane permeability; plasma proteins and blood cells enter the filtrate, causing increased urine volume due to increased osmotic concentration of the filtrate
Acute glomerulonephritis	Often occurs 1–3 weeks after a severe bacterial infection, such as strep throat; normally subsides after several days
Chronic glomerulonephritis	Long-term and progressive process whereby the filtration membrane thickens and is eventually replaced by connective tissue and the kidneys become nonfunctional
Renal Failure	Can result from any condition that interferes with kidney function
Acute renal failure	Occurs when damage to the kidney is rapid and extensive; leads to accumulation of wastes in the blood; can lead to death in 1–2 weeks if renal failure is complete
Chronic renal failure	Results from permanent damage to so many nephrons that the remaining nephrons are inadequate for normal kidney function; can be caused by chronic glomerulonephritis, trauma to the kidneys, tumors, or kidney stones

SUMMARY

The urinary system consists of two kidneys, two ureters, the urinary bladder, and the urethra.

18.1 Functions of the Urinary System

1. The kidneys excrete waste products.

2. The kidneys control blood volume and blood pressure by regulating the volume of urine produced.
3. The kidneys help regulate the concentration of major ions in the body fluids.
4. The kidneys help regulate the pH of the extracellular fluid.
5. The kidneys regulate the concentration of red blood cells in the blood.
6. The kidneys participate, with the skin and liver, in regulating vitamin D synthesis.

18.2 Anatomy of the Kidneys

Location and External Anatomy of the Kidneys

Each kidney is behind the peritoneum and surrounded by a renal capsule and adipose tissue.

Internal Anatomy and Histology of the Kidneys

1. The kidney is divided into an outer cortex and an inner medulla.
2. Each renal pyramid has a base located at the boundary between the cortex and the medulla. The tip of the renal pyramid extends toward the center of the kidney and is surrounded by a calyx.
3. Calyces are extensions of the renal pelvis, which is the expanded end of the ureter within the renal sinus.
4. The functional unit of the kidney is the nephron. The parts of a nephron are the renal corpuscle, the proximal convoluted tubule, the loop of Henle, and the distal convoluted tubule.
5. The filtration membrane is formed by the glomerular capillaries, the basement membrane, and the podocytes of the Bowman capsule.

Arteries and Veins

1. Renal arteries give rise to branches that lead to afferent arterioles.
2. Afferent arterioles supply the glomeruli.
3. Efferent arterioles carry blood from the glomeruli to the peritubular capillaries.
4. Blood from the peritubular capillaries flows to the renal veins.

18.3 Urine Production

Urine is produced by filtration, tubular reabsorption, and tubular secretion.

Filtration

1. The renal filtrate passes from the glomerulus into the Bowman capsule and contains no blood cells and few blood proteins.
2. Filtration pressure is responsible for filtrate formation.
3. Increased sympathetic activity decreases blood flow to the kidney, decreases filtrate formation, and decreases urine production. Decreased sympathetic activity has the opposite effect.

Tubular Reabsorption

1. About 99% of the filtrate volume is reabsorbed; 1% becomes urine.
2. Among the substances reabsorbed are proteins, amino acids, glucose, fructose, Na^+, K^+, Ca^{2+}, HCO_3^-, and Cl^-.
3. About 65% of the filtrate volume is reabsorbed in the proximal convoluted tubule, 15% is reabsorbed in the descending limb of the loop of Henle, and another 19% is reabsorbed in the distal convoluted tubule and collecting duct.

Tubular Secretion

Hydrogen ions, some by-products of metabolism, and some drugs are actively secreted into the nephron.

18.4 Regulation of Urine Concentration and Volume

Urine Concentration Mechanisms

1. The countercurrent mechanisms found in the loop of Henle and the vasa recta create a very high concentration of solutes in the interstitial fluid of the kidney.
2. The medullary concentration gradient created by the countercurrent mechanisms allows the kidney to concentrate water.
3. Water moves by osmosis out of the kidney tubules toward the high solute concentration of the interstitial fluid in the medulla of the kidney.

Hormonal Mechanisms

1. Renin is secreted from the kidney when the blood pressure decreases. Renin converts angiotensinogen to angiotensin I, which is then converted to angiotensin II by angiotensin-converting enzyme. Angiotensin II stimulates aldosterone secretion, and aldosterone increases the rate of Na^+ and Cl^- reabsorption from the nephron.
2. ADH is secreted from the posterior pituitary when the concentration of blood increases or when blood pressure decreases. ADH increases the permeability to water of the distal convoluted tubule and collecting duct. It increases water reabsorption by the kidney.
3. Atrial natriuretic hormone, secreted from the right atrium in response to increases in blood pressure, acts on the kidney to increase Na^+ and water loss in the urine.

18.5 Urine Movement

Anatomy and Histology of the Ureters, Urinary Bladder, and Urethra

1. Each ureter carries urine from a renal pelvis to the urinary bladder.
2. The urethra carries urine from the urinary bladder to the outside of the body.
3. The ureters and urinary bladder are lined with transitional epithelium and have smooth muscle in their walls.
4. The external urethral sphincter regulates the flow of urine through the urethra.

Micturition Reflex

1. Increased volume in the urinary bladder stretches its wall and activates the micturition reflex.
2. Parasympathetic action potentials cause the urinary bladder to contract. Reduced somatic motor action potentials cause the external urethral sphincter to relax.
3. Higher brain centers control the micturition reflex. Stretching of the urinary bladder stimulates sensory neurons that carry impulses to the brain and inform the brain of the need to urinate.

18.6 Body Fluid Compartments

1. Water and the ions dissolved in the water are distributed in the intracellular and extracellular fluid compartments.
2. Approximately two-thirds of the total body water is found within cells.
3. Approximately one-third of the total body water is found outside cells, mainly in interstitial fluid, blood plasma, and lymph.

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Composition of the Fluid in the Body Fluid Compartments

1. Intracellular fluid contains more K^+, Mg^{2+}, PO_4^{3-}, SO_4^{2-}, and protein than does extracellular fluid.
2. Extracellular fluid contains more Na^+, Ca^{2+}, Cl^-, and HCO_3^- than does intracellular fluid.

Exchange Between Body Fluid Compartments

Water moves continuously between compartments in response to hydrostatic pressure differences and osmotic differences between the compartments.

18.7 Regulation of Extracellular Fluid Composition

The total amount of water and electrolytes in the body does not change unless the person is growing, gaining weight, or losing weight.

Thirst Regulation

The sensation of thirst increases if extracellular fluid becomes more concentrated or if blood pressure decreases.

Ion Concentration Regulation

1. Sodium ions are the dominant extracellular ions. Aldosterone increases Na^+ reabsorption from the filtrate, ADH increases water reabsorption from the nephron, and ANH increases Na^+ loss in the urine.
2. Aldosterone increases K^+ secretion in the urine. Increased blood levels of K^+ stimulate, and decreased blood levels of K^+ inhibit, aldosterone secretion.
3. Parathyroid hormone secreted from the parathyroid glands increases extracellular Ca^{2+} levels by causing bone resorption and increased Ca^{2+}

uptake in the kidney. Parathyroid hormone increases vitamin D synthesis. Calcitonin, secreted by the thyroid gland, inhibits bone resorption and lowers blood Ca^{2+} levels when they are too high.

4. When PO_4^{3-} and SO_4^{2-} levels in the filtrate are low, nearly all PO_4^{3-} and SO_4^{2-} are reabsorbed. When levels are high, excess is lost in the urine.

18.8 Regulation of Acid-Base Balance

Regulation of Acid-Base Balance by Buffer Systems

Three principal classes of buffers in the body fluids resist changes in the pH: proteins, the phosphate buffer system, and the bicarbonate buffer system.

Regulation of Acid-Base Balance by the Respiratory System

The respiratory system rapidly regulates pH. An increased respiratory rate raises the pH because the rate of CO_2 elimination is increased, and a reduced respiratory rate reduces the pH because the rate of CO_2 elimination is reduced.

Regulation of Acid-Base Balance by the Kidneys

The kidneys excrete H^+ in response to a decreasing blood pH, and they reabsorb H^+ in response to an increasing blood pH.

Acidosis and Alkalosis

1. Acidosis occurs when the pH of the blood falls below 7.35. The two major types are respiratory acidosis and metabolic acidosis.
2. Alkalosis occurs when the pH of the blood increases above 7.45. The two major types are respiratory alkalosis and metabolic alkalosis.

REMEM BERING AND UNDERS

TANDING

1. Name the structures that make up the urinary system. List the functions of the urinary system.
2. What structures surround the kidney?
3. Describe the relationships of the renal pyramids, calyces, renal pelvis, and ureter.
4. What is the functional unit of the kidney? Name its parts.
5. Describe the blood supply to the kidney.
6. Name the three general processes involved in the production of urine.
7. Describe the filtration membrane. What substances do not pass through it?
8. How do changes in blood pressure in the glomerulus affect the volume of filtrate produced?
9. What effect does sympathetic stimulation have on the kidneys?
10. What substances are reabsorbed in the nephron? What happens to most of the filtrate volume that enters the nephron?
11. In what parts of the nephron are large volumes of filtrate reabsorbed? In what part of the nephron is no filtrate reabsorbed?
12. In general, what substances are secreted into the nephron?
13. What effect does ADH have on urine volume? Name the factors that cause an increase in ADH secretion.
14. Where is renin produced, and what stimulates its secretion?
15. Explain how renin controls the synthesis of angiotensin I. What enzyme regulates the conversion of angiotensin I to angiotensin II?
16. Describe the effect of angiotensin II on aldosterone secretion.
17. Where is aldosterone produced, and what effect does it have on urine volume? What factors stimulate aldosterone secretion?
18. Where is atrial natriuretic hormone produced, and what effect does it have on urine production?
19. What are the functions of the ureters, urinary bladder, and urethra? Describe their structure.

20. Describe the micturition reflex. How is voluntary control of micturition accomplished?
21. What stimuli result in an increased sensation of thirst?
22. Describe how Na^+ levels are regulated in the body fluids.
23. Describe how K^+ levels are regulated in the body fluids.
24. Describe how Ca^{2}+ levels are regulated in the body fluids.
25. Explain how buffers respond to changes in the pH of body fluids.
26. Explain how the respiratory system and the kidneys respond to changes in the pH of body fluids.
27. Define respiratory acidosis, metabolic acidosis, respiratory alkalosis, and metabolic alkalosis.

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CRITICAL THINKING

1. Thiago decided to do an experiment after reading the urinary system chapter in his favorite anatomy and physiology textbook. He drank 2 L of water in 15 min and then monitored his rate of urine production and urine concentration over the next 2 hours. What did he observe? Explain the major mechanism involved.
2. A student ate a full bag of salty (NaCl) potato chips but drank no liquids. What effect did this have on urine concentration and the rate of urine production? Explain the mechanisms involved.
3. During severe exertion in a hot environment, a person can lose up to 4 L of sweat per hour (sweat is less concentrated than extracellular fluid in the body). What effect would this loss have on urine concentration and rate of production? Explain the mechanisms involved.

4. Which of the following symptoms are consistent with reduced secretion of aldosterone: excessive urine production, low blood pressure, high plasma potassium levels, high plasma sodium levels? Explain.
5. Propose as many ways as you can to decrease the rate at which filtrate enters the Bowman capsule.
6. Lien Hua has an enteropathogenic *Escherichia coli* infection that causes severe diarrhea. Diarrhea produces a large volume of mucus that contains high concentrations of HCO_3^-. How would this diarrhea affect this patient's blood pH, urine pH, and respiration rate?
7. Sadiq and his mother went to a grocery store, where Sadiq eyed some candy he wanted. His mother refused to buy it, so Sadiq became angry. He held his breath for 2 min. What effect did this have on his body fluid pH? After the 2 min, what mechanisms were most important in reestablishing the normal body fluid pH?
8. Martha suffered from severe nausea for 2 days. She vomited frequently and was so nauseated that she could not tolerate eating or drinking anything. Explain how each of the following levels had changed in her body by the second day: blood pH, blood ADH, blood aldosterone, and urine pH.

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER

19

Reproductive System

Both male and female reproduction involve production of specialized cells that merge to form offspring.

LEARN TO APPLY IT

Chase and Christina were studying for their last anatomy and physiology exam of the semester. After reviewing his notes on meiosis, Chase said, "Well, since meiosis is the same in males and females, I don't need to study the meiosis notes from the female reproductive system lecture." Christina quickly pointed out that he was mistaken and that if he reviewed his notes he would see that meiosis is very different in males and females.

After reading chapter 19, explain the major differences between meiosis in males and meiosis in females. Describe any advantages to the differences between male and female meiosis.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

Module 14 Reproductive System

19.1 FUNCTIONS OF THE REPRODUCTIVE SYSTEM

Learning Outcome ***After reading this section, you should be able to***

A. List the functions of the male and female reproductive systems.

The human species could not survive without functional male and female reproductive systems. The reproductive systems play essential roles in the development of the structural and functional differences between males and females, influence human behavior, and produce offspring. However, a reproductive system, unlike other organ systems, is not necessary for the survival of an individual human.

Most of the body's organ systems show little difference between males and females, but the male and female reproductive systems exhibit striking differences. On the other hand, they have a number of similarities. For example, many reproductive organs of males and females are derived from the same embryological structures (see chapter 20), and some hormones are the same in males and females, even though they produce different responses. The reproductive system performs the following functions:

1. *Production of gametes.* The reproductive system produces gametes: sperm cells in the testes of males and oocytes (eggs) in the ovaries of females.
2. *Fertilization.* The reproductive system enhances fertilization of the oocyte by the sperm. The duct system in males nourishes sperm until they are mature and are deposited in the female reproductive tract by the penis. The female

reproductive system receives the male's sperm and transports them to the fertilization site.

3. *Development and nourishment of a new individual.* The female reproductive system nurtures the development of a new individual in the uterus until birth and provides nourishment (milk) after birth.
4. *Production of reproductive hormones.* Hormones produced by the reproductive system control its development and the development of the sex-specific body form. These hormones are also essential for the normal function of the reproductive system and for reproductive behavior.

19.2 FORMATION OF GAMETES

Learning Outcome *After reading this section, you should be able to*

A. Describe the function of meiosis in the formation of sperm cells and oocytes.

The testes in males and the ovaries in females (figure 19.1) produce **gametes** (GAM-eets), or *reproductive cells*. The formation of gametes in males and females occurs by a type of cell division called **meiosis** (my-OH-sis; a lessening) (see chapter 3).

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Figure 19.1 APR **Major Organs of the Reproductive System**

(*a*) The male reproductive system: testes, epididymides, ducta deferentia, seminal vesicles, prostate gland, and penis. (*b*) The female reproductive system: ovaries, uterine tubes, uterus, vagina, and mammary glands.

Meiosis occurs only in the testes of males and the ovaries of females. Before meiosis begins, all the chromosomes in these cells are duplicated, creating identical copies of each chromosome, called **chromatids.** Then, during meiosis, one cell divides twice to produce four daughter cells. During the first cell division of meiosis, the number of chromosomes in each cell is reduced from 46 (23 pairs) chromosomes to 23 total chromosomes. Therefore, the first cell division is called a *reduction division*. The steps in the second cell division of meiosis are comparable to those in mitosis. During the second cell division of meiosis, the chromatids of the 23 chromosomes in each cell are separated, producing four cells. Each cell contains half of their original chromosome number, or 23. This reduction in the number of chromosomes in each cell is critical. During sexual reproduction, two gametes (an egg and a sperm) merge to produce the offspring. If each gamete were to contain the original number of chromosomes, the offspring would contain far too many chromosomes and would not survive.

The two divisions of meiosis are called (1) meiosis I and (2) meiosis II. Like mitosis, each division of meiosis has prophase, metaphase, anaphase, and telophase.

Figure 19.2 details the steps in meiosis I and II.

PROCESS Figure

PROCESS Figure 19.2 APR Meiosis

During meiosis, the chromosome number is halved in preparation for sexual reproduction.

How many chromosomes would an oocyte contain if during anaphase II, the chromatids of one chromosome did not separate?

Meiosis I

❶ In early **prophase I,** at the beginning of meiosis, each of the 46 chromosomes consists of 2 chromatids connected by a centromere.

❷ In middle prophase I, the chromosomes align as pairs in a process called **synapsis** (si-NAP-sis; a connection). To picture chromosome pairs, find a pair of your shoes. These shoes match, but you probably could not comfortably wear them on the opposite feet. In much the same way, chromosome pairs have similar, but not identical, information. Now, to picture chromatids, imagine you bought two pairs of the same shoe. The two right shoes and the two left shoes represent the chromatids. Because each chromosome consists of 2 chromatids, the pairing of the chromosomes brings 2 chromatids of each chromosome close together. Occasionally, part of a chromatid of 1 chromosome breaks off and is exchanged with part of another chromatid from the other chromosome. This event, called **crossing over,** allows the exchange of genetic material between chromosomes.

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❸ In **metaphase I,** the chromosomes align along the center of the cell.

❹ In **anaphase I,** the pairs of chromosomes are separated to each side of the cell.

❺ During **telophase I**, new nuclei form and the cell divides. When meiosis I is complete, each daughter cell has 1 chromosome from each of the pairs, or 23 chromosomes. However, each of the 23 chromosomes in each daughter cell consists of 2 chromatids joined by a centromere.

Meiosis II

❻ In **prophase II,** the chromosomes each consist of 2 chromatids.

❼ In **metaphase II,** the chromosomes align along the center of the cell.

❽ In **anaphase II,** the chromatids separate at the centromere.

❾ In **telophase II,** each daughter cell receives 1 of the chromatids from each chromosome. When the centromere separates, each of the chromatids is

again called a chromosome. At the end of telophase II, there are 4 daughter cells, each containing 23 chromosomes.

During fertilization, the zygote receives 1 set of chromosomes (23) from each parent. Although half the genetic material of a zygote comes from each parent, the genetic makeup of each zygote is unique.

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CLINICAL IMPACT

Gender and Sex

At birth, people are assigned one of three biological sexes based solely on the anatomy of their external genitalia. Males have a penis, females have a vagina, and intersex people can have a wide variation in sexual characteristics. However, anatomy does not always dictate a person's gender identity. Gender identity is how people view and express themselves in the world. Biological sex also does not determine a person's sexual orientation. Sexual orientation is the interpersonal interactions people have with others with regard to physical, emotional, and romantic attraction. Sexual orientation also does not determine sexual preference. Sexual preference refers to the way a person wishes to receive and participate in physically intimate actions.

Until about the 1990s, the societal norm for humans in the United States consisted of a gender binary. The gender binary is the system of viewing gender as consisting of only two identities and two sexes: male and female. However, since the 1990s, it has been recognized that gender exists along a gender spectrum, sometimes referred to as nonbinary. The gender spectrum is a continuum of gender identity that includes male and female, but does not assert male and female as absolutes or as polar opposites. For parents of a gender-expansive child, one who goes against societal norms for gender identity, the first source of information is usually a medical professional. This means that physicians, nurses, and all medical professionals are put into a pivotal role of helping to provide understanding and resources to parents.

An immense set of terms exists to describe gender identity, sexual orientation, and sexual preference. Here, we provide a brief introduction to some of these terms:

1. Gender identity—how individuals view themselves; gender identity can be the same or different than the sex assigned to them at birth
2. Gender expression—how individuals present themselves in terms of appearance, behavior, clothing, haircut, etc.
3. Gender nonconforming—behaving in a way that does not conform to societal expectation of biological sex
4. Queer—a previously derogatory term used for certain sexual orientations, but now is used to express fluid identities and orientations; usually used by people who do

not identify as straight (heterosexual)

5. Transgender—individuals whose gender identity and/or gender expression is not the same as societal expectations based on their assigned biological sex. Although this does not imply a particular sexual orientation, it can be described as an FtM (F2M), female to male, transition or an MtF (M2F), a male to female, transition when individuals begin to express the knowledge of their internal identity by their outward appearance.
6. Gender dysphoria—the term used to describe the long-term distress individuals experience when their assigned biological sex does not align with their gender identity
7. Gay—the sexual attraction and affectional orientation between members of the same gender (assigned or expressed); refers to males and females
8. Pansexual—not limited in attraction to an individual with regard to biological sex, gender, or gender identity
9. Lesbian—the sexual attraction and affectional orientation between two females (assigned or expressed)
10. Bisexual—being sexually, emotionally, and physically attracted to people of both the same gender and another gender

19.3 MALE REPRODUCTIVE SYSTEM

Learning Outcomes ***After reading this section, you should be able to***

A. Describe the scrotum and its role in regulating the temperature of the testes.
B. Describe the structure of the testes.
C. Describe the specialized cells of the testes.
D. Describe the process of spermatogenesis.
E. Describe the ducts of the male reproductive system.
F. Describe the functions of the ducts of the male reproductive system.
G. Describe the structure of the penis, seminal vesicles, bulbourethral glands, and prostate gland.
H. Explain the function of the penis, seminal vesicles, bulbourethral glands, and prostate gland.

The male reproductive system consists of (1) the testes (sing. testis), (2) a series of ducts, which include the epididymides (sing. epididymis), the ducta deferentia (sing. ductus deferens; also, vas deferens), and the urethra, (3) accessory glands, which include the seminal vesicles, the prostate gland, and the bulbourethral glands, and (4) supporting structures, which include the scrotum and the penis (figure 19.3). The testes and epididymides, in which the sperm cells develop, are located outside the body cavity in the scrotum. Sperm cells travel from each testis through the ductus deferens to the prostate gland. Within the prostate gland, sperm cells enter the urethra. The urethra exits the pelvis, passes through the penis, and opens to the outside of the body.

Figure 19.3 APR **Male Reproductive Structures**

Medial view of the male pelvis, showing the male reproductive structures.

Scrotum

The **scrotum** (SKROH-tum) is a saclike structure containing the testes. It is divided into right and left internal compartments by an incomplete connective tissue septum. The wall of the scrotum includes the skin, a layer of loose connective tissue, and a layer of smooth muscle called the **dartos** (DAR-toss) **muscle.** In cold temperatures, the dartos muscle contracts, causing the skin of the scrotum to become firm and wrinkled and reducing its overall size. At the same time, the **cremaster** (kri-MAS-ter) **muscles** (see figure 19.6), which are extensions of abdominal skeletal muscles into the scrotum, contract and help pull the testes nearer the body. These changes in size and position of the scrotum help keep the testes warm. When temperature increases due to a warmer environment or as a result of exercise or fever, the dartos and cremaster muscles relax, and the skin of the scrotum becomes loose and thin, allowing the testes to descend away from the body and keep cool. The response of the dartos and cremaster muscles is important because sperm cells are very temperature-sensitive and do not develop normally if the testes become too warm or too cool.

CLINICAL IMPACT

Descent of the Testes

The testes develop in the abdominopelvic cavity. They move from the abdominopelvic cavity through the **inguinal** (IN-gwin-al; *inguen,* groin) **canal** to the scrotum. The inguinal canals and the internal layers of the scrotum originate as outpocketings of the abdominal cavity along the lateral, superior margin of the pubis. The descent of the testes occurs during the seventh or eighth month of fetal development or, in some cases, shortly after birth. **Cryptorchidism** (krip-TOR-kih-dizm) is the failure of one or both of the testes to descend into the scrotum. Because the higher temperature of the abdominal cavity prevents normal sperm cell development, sterility can result if both testes are involved (see chapter 20). In addition, approximately 10% of testicular cancer cases occur in males with a history of cryptorchidism. Fortunately, if the testis has not descended into the scrotum by the age of 4 months, it can be surgically repaired.

After the testes descend, the inguinal canals narrow permanently, but they remain as weak spots in the abdominal wall. An inguinal canal that enlarges or ruptures can result in an **inguinal hernia** (HER-nee-ah; rupture), through which a loop of intestine can protrude. This herniation can be quite painful and even very dangerous, especially if the inguinal canal compresses the intestine and cuts off its blood supply. Fortunately, inguinal hernias can be repaired surgically.

Testes

The **testes** (TES-tees), or male gonads (GOH-nads; *gonē,* seed), are oval organs, each about 4–5 cm long, within the scrotum (see figure 19.3). The outer part of each testis consists of a thick, white connective tissue capsule. Extensions of the capsule project into the interior of the testis and divide each testis into about 250 cone-shaped lobules (figure 19.4*a*). The lobules contain **seminiferous** (sem-ih-NIF-er-us) **tubules,** the site of sperm cell development. Located outside the seminiferous tubules are endocrine cells, called **interstitial** (in-ter-STISH-al) **cells,** or *Leydig* (LYE-dig) *cells*. Interstitial cells secrete testosterone.

Figure 19.4 **Structure of the Testis and Sperm Cell**

(*a*) Gross anatomy of the testis, with a section cut away to reveal the internal structures and histology. (*b*) Cross section of a seminiferous tubule. Spermatogonia are near the periphery, and mature sperm cells are near the lumen of the seminiferous tubules. (*c*) The regions of a mature sperm cell include the head, midpiece, and tail.

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Spermatogenesis

Spermatogenesis (SPER-mat-oh-JEN-eh-sis) is the formation of sperm cells. Before puberty, the testes remain relatively simple and unchanged from the time of their initial development. The interstitial cells are not prominent, and the seminiferous tubules are small and not yet functional. At 12–14 years of age, the interstitial cells increase in number and size, a lumen develops in each seminiferous tubule, and sperm cell production begins. It takes approximately 74 days for sperm cells to be produced. For about 50 of those days, the sperm cells are in the seminiferous tubules.

Spermatogenesis occurs in the seminiferous tubules. The seminiferous tubules contain two types of cells, (a) germ cells and (b) sustentacular cells. The **germ cells** are the ones that divide and differentiate during spermatogenesis to form sperm cells. The **sustentacular cells,** or *Sertoli* (ser-TOH-lee) *cells,* are large and extend from the periphery to the lumen of the seminiferous tubule (figure 19.4*b*). They nourish the germ cells and produce a number of hormones.

Figure 19.5 illustrates the steps in spermatogenesis.

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PROCESS Figure

PROCESS Figure 19.5 APR **Spermatogenesis**

A section of the seminiferous tubule illustrates the process of meiosis and sperm cell formation. The number in each cell indicates the total chromosome number.

Given that each secondary spermatocyte has 23 chromosomes, how is it possible that at the end of meiosis II, each of the four spermatids also have 23 chromosomes?

1. Germ cells are partially embedded in the sustentacular cells. The most peripheral cells, those adjacent to the basement membrane of the seminiferous tubules, are **spermatogonia** (SPER-mah-toh-GOH-nee-ah), which divide by mitosis. Some of the daughter cells produced from these mitotic divisions remain spermatogonia and continue to produce additional spermatogonia. Other daughter cells differentiate to form **primary spermatocytes** (SPER-mah-TOH-sytes), which divide by meiosis.
2. Recall that prior to meiosis, the chromosomes duplicate so that each of the 46 chromosomes is present in two copies, or chromatids. Thus, a primary spermatocyte contains 46 chromosomes, each consisting of 2 chromatids. Each primary spermatocyte completes the first meiotic division to produce 2 **secondary spermatocytes.**
3. Each secondary spermatocyte undergoes the second meiotic division to produce 2 smaller cells called **spermatids** (SPER-mah-tids). Each of the four spermatids has 23 chromosomes.
4. The spermatids undergo major structural changes to form mature sperm cells (see figure 19.4*b,c*). Much of the cytoplasm of the spermatids is eliminated, and each spermatid develops a head, midpiece, and flagellum (tail) to become a **sperm cell,** or *spermatozoon* (see figure 19.4*b–d*).

At the end of spermatogenesis, the developing sperm cells are located around the lumen of the seminiferous tubules, with their heads directed toward the surrounding sustentacular cells and their tails directed toward the center of the lumen (figure 19.5; see figure 19.4*b*). The head of the sperm cell contains the nucleus of the sperm cell. Just anterior to the nucleus is a vesicle called the **acrosome** (AK-roh-sohm), which contains enzymes that are released during the process of fertilization and are necessary for the sperm cell to penetrate the oocyte, or egg cell. Sperm cells are released into the lumen of the seminiferous tubules.

Ducts

After their production, sperm cells are transported through the seminiferous tubules and a series of ducts to the exterior of the body.

Epididymis

The seminiferous tubules of each testis converge into a tubular network called the **rete** (REE-teh; net) **testis** (see figure 19.4*a*). The rete testis empties into 15–20 tubules called the **efferent ductules** (EF-eh-rent DUCK-toolz). The efferent ductules carry sperm cells from the testis to a tightly coiled series of threadlike tubules that form a comma-shaped structure on the posterior side of the testis called the **epididymis** (EP-ih-DID-ih-miss) (figure 19.6; see figures 19.3 and 19.4). The sperm cells continue to mature within the epididymis, developing the capacity to swim and the ability to bind to the oocyte. Sperm cells taken directly from the testes are not capable of fertilizing oocytes, but after maturing for several days in the epididymis, the sperm cells develop the capacity to function as gametes. Final changes in sperm cells, called **capacitation** (kuh-PAS-i-tey-shun), occur after ejaculation of semen into the vagina and prior to fertilization.

Figure 19.6 APR **Male Reproductive Organs**

(*a*) Frontal view of a testis, an epididymis, and a ductus deferens, along with the penis and glands of the male reproductive system. The testis is viewed in the scrotal sac with the smooth muscle and cremaster muscles on one

side. The ductus deferens extends from the epididymis in the scrotal sac and passes through the inguinal canal and pelvic cavity to the prostate gland. Note that the ductus deferens and the testicular artery, vein, and nerves are surrounded by the cremaster muscle and connective tissue to form the spermatic cord. (*b*) A cross section of the penis illustrates the two dorsal corpora cavernosa and the ventral corpus spongiosum. Connective tissue sheaths and skin cover the three erectile bodies. Blood vessels, including the dorsal artery and vein, and the dorsal nerve of the penis are visible.

Ductus Deferens

The **ductus deferens** (DUK-tus DEH-fuh-renz, or *vas deferens,* is a tube that carries sperm from the testis into the body cavity of the male. The total length of the ductus deferens is about 45 cm (that's over 1 foot in length!). It emerges from the epididymis and ascends along the posterior side of the testis, where it becomes associated with the blood vessels and nerves that supply the testis to form the **spermatic cord** (figure 19.6*a*). Each spermatic cord consists of (1) the ductus deferens, (2) the testicular artery and veins, (3) lymphatic vessels, and (4) the testicular nerve. In addition, the spermatic cord is surrounded by the cremaster muscle and two connective tissue sheaths.

Each ductus deferens, and the rest of the spermatic cord structures, pass through the abdominal wall by way of the inguinal canal. Each ductus deferens then crosses the lateral wall of the pelvic cavity and loops behind the posterior surface of the urinary bladder. Near its end, the ductus deferens increases in diameter to become the **ampulla of the ductus deferens** (figure 19.6*a*). The wall of the ductus deferens contains smooth muscle, which contracts in peristaltic waves to propel the sperm cells from the epididymis to the ampulla.

Seminal Vesicle and Ejaculatory Duct

Near the ampulla of each ductus deferens is a sac-shaped gland called the **seminal vesicle** (SEM-in-al VES-ih-kull). A short duct extends from the seminal vesicle to the ampulla of the ductus deferens. The ducts from the seminal vesicle and the ampulla of the ductus deferens join at the prostate gland to form the **ejaculatory** (ih-JACK-you-leh-toh-ree) **duct.** Each ejaculatory duct enters the prostate gland and joins the urethra (figure 19.6*a*).

Urethra

The male **urethra** (you-REE-thra) extends from the urinary bladder to the distal end of the penis (figure 19.6*a*; see figure 19.3). The urethra can be divided into three parts: (1) the **prostatic urethra,** which passes through the prostate gland; (2) the **membranous urethra,** which passes through the floor of the pelvis and is surrounded by the external urinary sphincter;

and (3) the **spongy urethra,** which extends the length of the penis and opens at its end. The urethra is a passageway for both urine and male reproductive fluids. However, urine and the reproductive fluids do not typically exit the urethra at the same time. While male reproductive fluids are passing through the urethra, a sympathetic reflex causes the internal urinary sphincter to contract, which keeps semen from passing into the urinary bladder and prevents urine from entering the urethra.

Penis

The **penis** (PEE-nis) is the male organ of copulation and functions in the transfer of sperm cells from the male to the female. The penis contains three columns of erectile tissue (figure 19.6). Engorgement of this erectile tissue with blood causes the penis to enlarge and become firm, a process called **erection** (ee-REK-shun). Two columns of erectile tissue form the dorsal portion and the sides of the penis and are called the **corpora cavernosa** (KOHR-pohr-ah kav-er-NOS-ah). The third, smaller erectile column occupies the ventral portion of the penis and is called the **corpus spongiosum** (KOHR-pus spun-gee-OH-sum). It expands over the distal end of the penis to form a cap, the **glans** (glanz) **penis.** The spongy urethra passes through the corpus spongiosum, including the glans penis, and opens to the exterior as the **external urethral orifice.**

The shaft of the penis is covered by skin that is loosely attached to the connective tissue surrounding the penis. The skin is firmly attached at the base of the glans penis, and a thinner layer of skin tightly covers the glans penis. The skin of the penis, especially the glans penis, is well supplied with sensory receptors. A loose fold of skin, called the **prepuce** (PREE-puce), or *foreskin,* covers the glans penis (see figure 19.3). **Circumcision** (ser-kum-SIZH-un) is the surgical removal of the prepuce, usually shortly after birth. There are few compelling medical reasons for circumcision. Uncircumcised males have a higher incidence of penile cancer, but the underlying causes seem related to chronic infections and poor hygiene. In those few cases in which the prepuce is "too tight" to be moved over the glans penis, circumcision can be necessary to avoid chronic infections and maintain normal circulation.

Glands

The seminal vesicles are glands consisting of many saclike structures located next to the ampulla of the ductus deferens (figure 19.6*a*; see figure 19.3). There are two seminal vesicles. Each is about 5 cm long and tapers into a

short duct that joins the ampulla of the ductus deferens to form the ejaculatory duct, as previously mentioned.

The **prostate** (PROS-tate) **gland** consists of both glandular and muscular tissue and is about the size and shape of a walnut (figure 19.6*a*; see figure 19.3). The prostate gland surrounds the urethra and the two ejaculatory ducts. It consists of a capsule and numerous partitions. The cells lining the partitions secrete prostatic fluid. There are 10–20 short ducts (not seen in figure 19.6*a*) that carry secretions of the prostate gland to the prostatic urethra.

Understand

Apply It 1

Changes in the size and texture of the prostate gland can be an indication of developing prostate cancer. Suggest a way that the size and texture of the prostate gland can be examined by palpation without surgical techniques (see figure 19.3).

The **bulbourethral** (BUL-boh-you-REE-thral) **glands,** or *Cowper glands,* are a pair of small, mucus-secreting glands located near the base of the penis (figure 19.6*a*; see figure 19.3). In young adults, each is about the size of a pea, but they decrease in size with age. A single duct from each gland enters the urethra. Just before ejaculation, the bulbourethral glands produce a mucous secretion that aids in sperm movement and survival as the sperm enter the female reproductive tract.

Secretions

Semen (SEE-men) is a mixture of sperm cells and secretions from the male reproductive glands. The seminal vesicles produce about 60% of the fluid, the prostate gland contributes approximately 30%, the testes contribute 5%, and the bulbourethral glands contribute 5%.

Testes, Bulbourethral Glands, and Urethra

The mucous secretions from the bulbourethral glands and the mucous glands of the urethra have four primary functions: (1) lubrication of the urethra for sperm movement, (2) neutralization of acidic fluid in the urethra, (3) some lubrication during intercourse, and (4) neutralization of acidity in the vagina.

Seminal Vesicles

The thick, mucuslike secretion of the seminal vesicles contains many substances, each with a unique function. The functions of these substances

include:

1. *Nourishment of sperm cells*. Fructose within the seminal vesicle secretions and other nutrients nourish the sperm cells as they move through the female reproductive tract.
2. *Coagulation of semen*. After ejaculation, coagulation proteins help thicken the semen, which keeps the sperm cells in the vagina for a longer period of time.
3. *Movement of sperm cells*. Prostaglandins in the seminal vesicle secretions stimulate smooth muscle contractions of the female reproductive tract to propel sperm cells through the tract.

Prostate Gland

The thin, milky secretions of the prostate also have several functions.

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1. *Regulate pH*. The pH of the prostate secretions is alkaline. The alkaline pH neutralizes the acidity of the male urethra, the secretions of the testes, the secretions of the seminal vesicles, and the vagina. This neutralization is important for normal sperm cell function. Sperm cells require a pH between 6.0 and 6.5 for optimal movement. Because the pH of vaginal secretions is between 3.5 and 4.0, sperm cells would not be able to swim to the oocyte without the alkaline pH of the prostate secretions.
2. *Aid in sperm cell travel to oocyte.* The prostate secretions are important in the temporary coagulation of semen because the secretions contain clotting factors. The coagulated semen remains a sticky mass for a few minutes after ejaculation, and then an enzyme, also secreted by the prostate, causes the mass to dissolve. This slowly releases the sperm cells to swim up the female reproductive tract to the oocyte.

The normal volume of semen is 2–5 milliliters (mL), with each milliliter of semen typically containing about 100 million sperm cells.

19.4 PHYSIOLOGY OF MALE REPRODUCTION

Learning Outcomes ***After reading this section, you should be able to***

A. List the hormones that influence the male reproductive system.
B. Describe the functions of the male reproductive hormones.
C. Describe the changes that occur in males during puberty.
D. Explain the events that occur during the male sexual act.

The male reproductive system depends on both hormonal and neural mechanisms to function normally. Hormones control (1) the development of reproductive structures, (2) the development of secondary sexual characteristics, (3) spermatogenesis, and (4) some aspects of sexual behavior. The mature neural mechanisms are primarily involved in (1) controlling the sexual act and (2) the expression of sexual behavior.

Regulation of Reproductive Hormone Secretion

The hypothalamus of the brain, the anterior pituitary gland, and the testes all produce hormones that influence the male reproductive system. Figure 19.7 illustrates the hormonal regulation of male reproduction.

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PROCESS Figure

PROCESS Figure 19.7 Regulation of Reproductive Hormone Secretion in Males

Male reproductive hormones are produced by the hypothalamus, the anterior pituitary, and the testes.

Suppose an adult male developed a tumor in one of his testes that resulted in abnormally high levels of testosterone. What would happen to his levels of GnRH, FSH, and LH?

1. **Gonadotropin-releasing** (GOH-nad-oh-TROH-pin) **hormone (GnRH)** is released from neurons in the hypothalamus and travels to the anterior pituitary gland (table 19.1). GnRH causes cells in the anterior pituitary gland to secrete two hormones, referred to as **gonadotropins** (GOH-nad-oh-TROH-pinz) because they influence the function of the **gonads** (GOH-nadz; testes or ovaries). The two gonadotropins are (a) **luteinizing** (LOO-tee-in-eye-zing) **hormone (LH)** and (b) **follicle-stimulating hormone (FSH).** LH and FSH are named for their functions in females, but they are also essential reproductive hormones in males.
2. LH binds to the interstitial cells in the testes and causes them to secrete testosterone.
3. FSH binds primarily to sustentacular cells in the seminiferous tubules and promotes sperm cell development. It also increases the secretion of a hormone called **inhibin** (in-HIB-in; to inhibit).
4. Testosterone has a stimulatory effect on the sustentacular cells of the seminiferous tubules, as well as on the development of reproductive organs and secondary sexual characteristics.
5. The blood levels of reproductive hormones are under negative-feedback control. Testosterone has a negative-feedback effect on the secretion of GnRH from the hypothalamus and the secretion of LH and FSH from the anterior pituitary gland.
6. Inhibin has a negative-feedback effect on the secretion of FSH from the anterior pituitary gland.

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Table 19.1 Major Reproductive Hormones in Males and Females

Hormone	Source	Target Tissue	Response
Male Reproductive System			
Gonadotropin-releasing hormone (GnRH)	Hypothalamus	Anterior pituitary	Stimulates secretion of LH and FSH
Luteinizing hormone (LH)	Anterior pituitary	Interstitial cells of the testes	Stimulates synthesis and secretion of testosterone

Hormone	Source	Target Tissue	Response
Follicle-stimulating hormone (FSH)	Anterior pituitary	Seminiferous tubules (sustentacular cells)	Supports spermatogenesis and inhibin secretion
Testosterone	Interstitial cells of testes	Testes; body tissues	Development and maintenance of reproductive organs; supports spermatogenesis and causes the development and maintenance of secondary sexual characteristics
		Anterior pituitary and hypothalamus	Inhibits GnRH, LH, and FSH secretion through negative feedback
Inhibin	Sustentacular cells	Anterior pituitary	Inhibits FSH secretion through negative feedback
Female Reproductive System			
Gonadotropin-releasing hormone (GnRH)	Hypothalamus	Anterior pituitary	Stimulates secretion of LH and FSH
Luteinizing hormone (LH)	Anterior pituitary	Ovaries	Causes follicles to complete maturation and undergo ovulation; causes ovulation; causes the ovulated follicle to become the corpus luteum
Follicle-stimulating hormone (FSH)	Anterior pituitary	Ovaries	Causes follicles to begin development
Estrogen	Follicles of ovaries and corpus luteum	Uterus	Proliferation of endometrial cells
		Breasts	Development of mammary glands (especially duct systems)

Hormone	Source	Target Tissue	Response
		Anterior pituitary and hypothalamus	Positive feedback before ovulation, resulting in increased LH and FSH secretion; negative feedback with progesterone on the hypothalamus and anterior pituitary after ovulation, resulting in decreased LH and FSH secretion
		Other tissues	Development and maintenance of secondary sexual characteristics
Progesterone	Corpus luteum of ovaries	Uterus	Enlargement of endometrial cells and secretion of fluid from uterine glands; maintenance of pregnant state
		Breasts	Development of mammary glands (especially alveoli)
		Anterior pituitary	Negative feedback, with estrogen, on the hypothalamus and anterior pituitary after ovulation, resulting in decreased LH and FSH secretion
		Other tissues	Secondary sexual characteristics
Oxytocin	Posterior pituitary	Uterus and mammary glands	Contraction of uterine smooth muscle and contraction of cells in the breast, resulting in milk letdown in lactating females
Human chorionic gonadotropin	Placenta	Corpus luteum of ovaries	Maintains corpus luteum and increases its rate of progesterone secretion during the first one-third (first trimester) of pregnancy; increases testosterone production in testes of male fetuses

For GnRH to stimulate LH and FSH release, the pituitary gland must be exposed to a series of brief increases and decreases in GnRH. If GnRH is maintained at a high level in the blood for days or weeks, the anterior pituitary cells become insensitive to it. GnRH can be produced synthetically and is useful in treating some people who are infertile. Synthetic GnRH must be administered in small amounts in frequent pulses or surges. GnRH can also inhibit reproduction because long-term administration of GnRH can sufficiently reduce LH and FSH levels to prevent sperm cell production in males or ovulation in females.

Puberty in Males

Puberty (PYU-ber-tee) is the time period during which individuals become capable of sexual reproduction. The reproductive system matures and assumes its adult functions, and the structural differences between adult males and females become more apparent. In males, puberty commonly begins between the ages of 12 and 14 and is largely completed by age 18. Before puberty, small amounts of testosterone, secreted by the testes and the adrenal cortex, inhibit GnRH, LH, and FSH secretion. Beginning just before puberty and continuing throughout puberty, developmental changes in the hypothalamus cause the hypothalamus and the anterior pituitary gland to become much less sensitive to the inhibitory effect of testosterone and the rate of GnRH, LH, and FSH secretion increases. Consequently, elevated FSH levels promote spermatogenesis, and elevated LH levels cause the interstitial cells to secrete larger amounts of testosterone. Testosterone still has a negative-feedback effect on the hypothalamus and anterior pituitary gland, but GnRH, LH, and FSH secretion occurs at substantially higher levels.

Effects of Testosterone

Testosterone (tes-TOSS-ter-ohn) is the major male hormone secreted by the testes. Testosterone influences reproductive organs and nonreproductive structures (table 19.2). During puberty, testosterone causes the enlargement and differentiation of the male genitals and the reproductive duct system. It is necessary for spermatogenesis and for the development of male secondary sexual characteristics. The **secondary sexual characteristics** are those structural and behavioral changes, other than in the reproductive organs, that develop at puberty and distinguish males from females. Secondary sexual characteristics in males include (1) hair distribution and growth, (2) skin texture, (3) body fat distribution, (4) skeletal muscle growth, and (5) changes in the larynx. After puberty, testosterone maintains the adult structure of the male genitals, reproductive ducts, and secondary sexual characteristics.

Table 19.2	Effects of Testosterone on Target Tissues
Target Tissue	**Response**
Penis and scrotum	Enlargement and differentiation
Hair follicles	Hair growth and coarser hair in the pubic area, legs, chest, axillary region, face, and occasionally back; pattern baldness on the head if the person has the appropriate genetic makeup
Skin	Coarser texture of skin; increased rate of secretion of sebaceous glands, frequently resulting in acne at the time of puberty; increased secretion of sweat glands in axillary regions
Larynx	Enlargement of larynx and deeper masculine voice
Most tissues	Increased rate of metabolism
Red blood cells	Increased rate of red blood cell production; a red blood cell count increase by about 20% as a result of increased erythropoietin secretion
Kidneys	Retention of sodium and water to a small degree, resulting in increased extracellular fluid volume
Skeletal muscle	A skeletal muscle mass increase at puberty; average increase is greater in males than in females
Bone	Rapid bone growth, resulting in increased rate of growth and early cessation of bone growth; males who mature sexually at a later age do not exhibit a rapid period of growth, but they grow for a longer time and can become taller than males who mature earlier

Male Sexual Behavior and the Male Sex Act

Testosterone is required for normal sexual behavior. Testosterone enters certain cells within the brain, especially within the hypothalamus, and influences their functions. The blood levels of testosterone remain relatively constant throughout the lifetime of a male, from puberty until about 40 years of age. Thereafter, the levels slowly decline to approximately 20% of this value by 80 years of age, causing a slow decrease in sex drive and fertility.

Apply It 2

What will be the effect on secondary sexual characteristics, external genitalia, and sexual behavior if the testes fail to produce normal amounts of testosterone at puberty?

The male sex act is a complex series of reflexes that result in erection of the penis, secretion of mucus into the urethra, emission, and ejaculation. **Emission** (ih-MISH-uhn) is the movement of sperm cells, mucus, prostatic secretions, and seminal vesicle secretions into the prostatic, membranous, and spongy urethra. **Ejaculation** (ee-JACK-you-LAY-shun) is the forceful expulsion of the secretions that have accumulated in the urethra to the exterior. Sensations, normally interpreted as pleasurable, occur during the male sex act and result in an intense sensation called an **orgasm** (OR-gaz-um), or *climax*. In males, orgasm is closely associated with ejaculation, although they are separate functions and do not always occur simultaneously. A phase called **resolution** occurs after ejaculation. During resolution, the penis becomes flaccid, an overall feeling of satisfaction exists, and the male is unable to achieve erection and a second ejaculation.

Sensory Impulses and Integration

Sensory action potentials from the genitals are carried to the sacral region of the spinal cord, where reflexes that result in the male sex act are integrated. Action potentials also travel from the spinal cord to the cerebrum to produce conscious sexual sensations.

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Rhythmic massage of the penis, especially the glans, and surrounding tissues, such as the scrotal, anal, and pubic regions, provide important sources of sensory action potentials. Engorgement of the prostate gland and seminal vesicles with secretions or irritation of the urethra, urinary bladder, ducta deferentia, and testes can also cause sexual sensations.

Psychological stimuli, such as sight, sound, odor, or thoughts, have a major effect on male sexual reflexes. Ejaculation while sleeping (nocturnal emission) is a relatively common event in young males and is thought to be triggered by psychological stimuli associated with dreaming.

Erection, Emission, and Ejaculation

When **erection** occurs, the penis becomes enlarged and rigid. Erection is the first major component of the male sex act. Neural stimuli, specifically, parasympathetic action potentials from the sacral region of the spinal cord, cause arteries supplying blood to the erectile tissues to dilate. Blood then fills small venous sinuses called **sinusoids** in the erectile tissue. The erectile tissues compress veins in the penis, restricting outflow of blood, which increases blood pressure within the penis. The increased blood pressure in the sinusoids causes the erectile tissue to become inflated and rigid.

Parasympathetic action potentials also cause the mucous glands within the urethra and the bulbourethral glands to secrete mucus.

Failure to achieve erections, or **erectile dysfunction (ED),** sometimes called *impotence,* can be a major source of frustration. The inability to achieve erections can be due to reduced testosterone secretion resulting from hypothalamic, pituitary, or testicular complications. In other cases, ED can be due to defective stimulation of the erectile tissue by nerve fibers or reduced response of the blood vessels to neural stimulation. Some males can achieve erections by taking oral medications, such as sildenafil (Viagra), tadalafil (Cialis), or vardenafil (Levitra), or by having specific drugs injected into the base of the penis. These drugs increase blood flow into the erectile tissue of the penis, resulting in erection for many minutes.

Before ejaculation, the ductus deferens begins to contract rhythmically, propelling sperm cells and testicular fluid from the epididymis through the ductus deferens. Contractions of the ductus deferens, seminal vesicles, and ejaculatory ducts cause the sperm cells, testicular secretions, and seminal fluid to move into the urethra, where they mix with prostatic secretions released by contraction of the prostate.

Emission is the accumulation of sperm cells and semen in the urethra. It is stimulated by sympathetic action potentials that originate in the lumbar region of the spinal cord. Action potentials cause the reproductive ducts to contract and stimulate the seminal vesicles and the prostate gland to release secretions. Consequently, semen accumulates in the urethra.

Ejaculation is the forceful release of semen from the urethra. It results from the contraction of smooth muscle in the wall of the urethra and skeletal muscles surrounding the base of the penis. Just before ejaculation, action potentials are sent to the skeletal muscles that surround the base of the penis. Rhythmic contractions are produced that force the semen out of the urethra, resulting in ejaculation. Muscle tension increases throughout the body as well.

Infertility in Males

Infertility (in-fer-TIL-i-tee) is the inability or the reduced ability to produce offspring. The most common cause of infertility in males is a low sperm cell count. A count of less than 20 million sperm cells per milliliter usually indicates infertility.

The sperm cell count can decrease because of damage to the testes as a result of trauma, radiation, cryptorchidism, or an infection, such as mumps. Reduced sperm cell counts can also result from inadequate secretion of LH and FSH, which can be caused by hypothyroidism, trauma to the

hypothalamus, damage to the hypothalamus or anterior pituitary gland, or tumors. Decreased testosterone secretion reduces the sperm cell count as well. Some reports suggest that the average sperm cell count has decreased substantially since the end of World War II (1945), although there is some controversy about the accuracy of these reports. Researchers speculate that certain synthetic chemicals are responsible.

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CLINICAL IMPACT

Pattern Baldness

Some males have a genetic tendency called **pattern baldness,** which develops in response to testosterone and other androgens. When testosterone levels increase at puberty, the density of hair on top of the head begins to decrease. Baldness usually reaches its maximum rate of development when the individual is in the third or fourth decade of life. Minoxidil (mi-NOKS-si-dil; Rogaine) is a drug that effectively prevents a decrease in hair growth in many males who exhibit male pattern baldness. It is most effective in those who are young and just starting to show evidence of baldness. Minoxidil causes blood vessels to dilate, including those close to hair follicles, which may explain how it works. However, the mechanism has not been confirmed.

Even when the sperm cell count is normal, fertility can be reduced if sperm cell structure is abnormal, as occurs due to chromosomal abnormalities or other genetic factors. Reduced sperm cell motility also results in infertility. A major cause of reduced sperm cell motility is the presence of anti-sperm antibodies, which are produced by the immune system and bind to sperm cells.

In cases of infertility due to low sperm count or reduced motility, fertility can sometimes be achieved by collecting several ejaculations and concentrating the sperm cells before inserting them into the female reproductive tract, a process called **artificial insemination** (in-sem-i-NAY-shun).

19.5 FEMALE REPRODUCTIVE SYSTEM

Learning Outcomes *After reading this section, you should be able to*

A. Name the organs of the female reproductive system.
B. Describe the structure of the organs of the female reproductive tract.
C. Describe the anatomy and histology of the ovaries.
D. Discuss the development of the oocyte and the follicle.
E. Describe ovulation and fertilization.
F. Describe the structure of the uterine tubes, uterus, vagina, external genitalia, and mammary glands.

The female reproductive organs consist of (1) the ovaries, (2) the uterine tubes (or fallopian tubes), (3) the uterus, (4) the vagina, (5) the external genitalia, and (6) the mammary glands (see figure 19.1*b*). The internal reproductive organs of the female are located within the pelvis, between the urinary bladder and the rectum (figure 19.8). The uterus and the vagina are in the midline, with an ovary to each side of the uterus (figure 19.9). The internal reproductive organs are held in place within the pelvis by a group of ligaments. The most conspicuous is the **broad ligament,** which spreads out on both sides of the uterus and attaches to the ovaries and uterine tubes.

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Figure 19.8 APR **Female Pelvis**

The female reproductive tract, including the uterus, the vagina, and the surrounding pelvic structures, is shown in a medial view of the female pelvis. Note that the female reproductive and urinary tracts open separately to the exterior.

Ovaries

Females have two **ovaries** (OH-va-rees; *ovum,* egg). Each ovary is a small organ suspended in the pelvic cavity by two ligaments. The **suspensory ligament** extends from each ovary to the lateral body wall. The **ovarian ligament** attaches the ovary to the superior margin of the uterus (figure 19.9). In addition, the ovaries are attached to the posterior surface of the broad ligament by folds of peritoneum called the **mesovarium** (MEZ-oh-VAR-e-um). The ovarian arteries, veins, and nerves traverse the suspensory ligament and enter the ovary through the mesovarium.

Figure 19.9 APR **Female Reproductive Organs**

Anterior view of the uterus, uterine tubes, and associated ligaments. The uterus and uterine tubes are cut in section (on the left side), and the vagina is cut to show the internal anatomy. The inset shows the relationships among the ovary, the uterine tube, and the ligaments that suspend them in the pelvic cavity.

A layer of visceral peritoneum covers the surface of the ovary. The outer part of the ovary is composed of dense connective tissue and contains **ovarian follicles** (figure 19.10). Each of the ovarian follicles contains an **oocyte** (OH-oh-site; *ōon,* egg), the female reproductive cell. Loose connective tissue makes up the inner part of the ovary, where blood vessels, lymphatic vessels, and nerves are located.

Figure 19.10 APR **Structure of the Ovary and Ovarian Follicles**

The ovary is sectioned to illustrate its internal structure (inset shows plane of section). Represented are ovarian follicles from each major stage of development, as well as a corpus luteum.

Oogenesis, Follicle Development, and Fertilization

The process of gamete production in females is called **oogenesis.** Oogenesis begins even before a female is born. By the fourth month of development, the ovaries contain 5 million **oogonia** (oh-oh-GOH-nee-ah), the cells from which oocytes develop. By the time a female infant is born, many of her oogonia have degenerated, while those remaining have differentiated into cells that have begun meiosis. Also, some data indicate that oogonia can form

after birth from stem cells, but the extent to which this occurs, and how long it occurs, is not clear. As in meiosis in males, the genetic material is duplicated, and two cell divisions occur (see section 19.2, “Formation of Gametes” earlier in this chapter). Figure 19.11 outlines the process of oogenesis.

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PROCESS Figure

PROCESS Figure 19.11 APR Maturation of the Oocyte and Follicle

The events leading to oocyte and follicle maturation are closely linked. Once these structures are mature, fertilization can result. The numbers written in the cells are total numbers of chromosomes.

Understand If the secondary oocyte is not fertilized after ovulation, what happens to it?

❶ Oogonia give rise to oocytes. Before birth, oogonia multiply by mitosis. During development of the fetus, many oogonia differentiate into cells that begin meiosis. Meiosis stops, however, during the first meiotic division at prophase I. The cell at this stage is called a **primary oocyte,** and at birth there are about 2 million of them. The primary oocytes remain stopped in prophase I until puberty.

❷ Before birth, the primary oocytes become surrounded by a single layer of flat cells, called granulosa cells, creating a primordial follicle. Primordial follicles are present until puberty. From birth to puberty, many primary oocytes degenerate. The number of primary oocytes decreases to around 300,000 to 400,000; of these, only about 400 will complete development and be released from the ovaries. Nearly all others degenerate after partial development.

❸ After puberty, primordial follicles develop into primary follicles. In a primary follicle, the oocyte enlarges and the single layer of granulosa cells becomes enlarged and cuboidal. Subsequently, several layers of granulosa cells form, and a layer of clear material called the **zona pellucida** (ZOH-nah pe-LOO-si-da) is deposited around the primary oocyte.

❹ The primary follicle becomes a **secondary follicle** as fluid-filled spaces called **vesicles** form among the granulosa cells, and a capsule called the **theca** (THEE-kah; a box) forms around the follicle.

❺ The secondary follicle continues to enlarge, and when the fluid-filled vesicles fuse to form a single, fluid-filled chamber called the **antrum** (AN-trum) the follicle is called the **mature follicle,** or *graafian* (GRAF-ee-an) *follicle*. The primary oocyte is pushed off to one side and lies in a mass of granulosa cells called the **cumulus cells.**

❻ **Ovulation** is the release of the **secondary oocyte** from the ovary. Just before ovulation, the primary oocyte completes the first meiotic division to produce a secondary oocyte and a nonviable **polar body.** Unlike meiosis in males, cytoplasm is not split evenly between the two cells. Most of the cytoplasm of the primary oocyte remains with the secondary oocyte. The polar body either degenerates or divides to form two polar bodies.

7. The secondary oocyte begins the second meiotic division but stops in metaphase II.
8. During ovulation, the secondary oocyte is released from the ovary. The mature follicle forms a lump on the surface of the ovary. During ovulation, the mature follicle ruptures, forcing a small amount of blood, follicular fluid, and the secondary oocyte, surrounded by the cumulus cells, into the peritoneal cavity. In most cases, only one of the follicles that begin to develop forms a mature follicle and undergoes ovulation. The other follicles degenerate.
9. The secondary oocyte completes meiosis II only if it is fertilized by a sperm cell. The completion of meiosis II forms an oocyte and a second polar body. **Fertilization** (FER-til-eye-ZAY-shun) begins when a sperm cell penetrates the cytoplasm of a secondary oocyte. Fertilization is complete when the oocyte nucleus and the sperm cell nucleus unite, returning the chromosome number to 46. This forms a **zygote** (ZIE-goht). The zygote has 23 pairs of chromosomes. All cells of the human body contain 23 pairs of chromosomes, except for the male and female gametes. The zygote divides by mitosis to form 2 cells, which divide to form 4 cells, and so on. The mass of cells formed may eventually implant in, or attach to, the uterine wall and develop into a new individual (see chapter 20).
10. In the ovary, following ovulation, the remaining cells of the ruptured follicle are transformed into a glandular structure called the **corpus luteum** (KOR-pus, body; LOO-tee-um, yellow). If pregnancy occurs, the corpus luteum enlarges in response to a hormone secreted by the placenta called **human chorionic gonadotropin hormone (hCG)** (koh-ree-ON-ik GOH-nad-oh-TROH-pin) (see table 19.1).
11.

If pregnancy does not occur, the corpus luteum lasts for 10–12 days and then begins to degenerate to form a remnant of the corpus luteum, called the corpus albicans. Although the timing varies considerably from person to person, in this textbook we assume that ovulation proceeds on a 28-day cycle.

MICROBES IN YOUR BODY

Human Papillomavirus and Cancer

In the majority of the "Microbes in Your Body" features, we have focused on bacteria. However, recall from chapter 1 that the human microbiota also includes viruses, protists, and fungi. Human papillomaviruses (HPV) belong to a family of DNA viruses that are naturally found on the skin soon after birth. Over 200 types of HPV have been identified, and most are not harmful. However, more than 10 types have been shown to be oncogenic, or cancer-causing, with two types, HPV 16 and HPV 18, being linked to 70% of all cervical cancer cases. In addition, the number of cases of mouth and throat cancers caused by HPV is on the rise, especially in males.

Viruses take over their host cell's machinery to replicate and form thousands of new individual viruses. In the case of HPV, the virus targets undifferentiated cells in the stratified squamous epithelium of the outer body skin, as well as the stratified squamous epithelium of the mucosal lining of the reproductive tract or pharynx (see chapter 4). Once the virus is inside the host cell nucleus, its DNA is replicated at the same time the host cell DNA is replicated. HPV induces uncontrolled division in its host's cells. The continued division causes an accumulation of mutations, and eventually the cell becomes cancerous. New HPV are released through normal shedding of cells. Fortunately, full-blown metastasizing cancer from an HPV infection takes more than 10 years to develop, which gives enough time for screening, identification, and treatment.

Because HPV is present for years with no clinical symptoms, the most effective way to avoid the oncogenic forms is to be vaccinated against them. Acquisition of HPV is often through sexual transmission, but the virus can also be passed from mother to child or from very close contact with an infected individual, such as providing personal hygienic care. Even so, HPV is the most common sexually transmitted disease, with some high-risk types. The high-risk types can develop into cervical cancer or several forms of head and neck cancers, particularly oropharyngeal cancer. In addition, naturally acquired HPV does not usually elicit a strong immune response, which prevents memory immune response to protect from potential future exposures. Thus, the vaccine Gardasil® has been developed to vaccinate against HPV types 16 and 18. Additional HPV vaccines also protect against several other types of HPV. Vaccination for all preteens and previously unvaccinated people through age 26 is recommended by the Centers for Disease Control and Prevention.

Recently, the Food and Drug Administration approved an HPV screening test for use in combination with the traditional Pap test for females. The Pap test involves collecting cells from the surface of the cervix for examination under a microscope. If the cells are abnormally shaped, as precancerous or cancerous cells would be, it is indicative that further testing should be done. However, the Pap test can be negative for abnormal cells even if the female has HPV. If that is the case, the HPV test is recommended to test if HPV is present. The HPV test is also recommended for females over 30 years of age even if the individual has been vaccinated for HPV, since the vaccine does not target all oncogenic forms of HPV. Eventually, with continued vaccination, the oncogenic types may become less relevant to human health.

Apply It 3

The identity of the cell surface receptors used by HPV to enter their host cell has not been completely identified but will most likely be known within the next several years. Propose a future mechanism that could use the cell surface receptor protein to prevent HPV uptake and the subsequent development of cancer-inducing uncontrolled cell division.

Uterine Tubes

A **uterine tube,** also called a *fallopian* (fa-LOH-pee-an) *tube* or *oviduct* (OH-vi-duct), is associated with each ovary. The uterine tubes extend from the area of the ovaries to the uterus. They open directly into the peritoneal cavity near each ovary and receive the secondary oocyte. The opening of each uterine tube is surrounded by long, thin processes called **fimbriae** (FIM-bree-ee; fringes) (see figure 19.9).

The fimbriae nearly surround the surface of the ovary. As a result, as soon as the secondary oocyte is ovulated, it comes into contact with the surface of the fimbriae. Cilia on the fimbriae surface sweep the oocyte into the uterine tube. Fertilization usually occurs in the part of the uterine tube near the ovary, called the **ampulla** (am-PUL-lah). The fertilized oocyte then travels to the uterus, where it embeds in the uterine wall in a process called **implantation.**

Uterus

The **uterus** (YOU-ter-us; womb) is as big as a medium-sized pear (see figures 19.8 and 19.9). It is oriented in the pelvic cavity with the larger, rounded part directed superiorly. The part of the uterus superior to the entrance of the uterine tubes is called the **fundus** (FUN-dus). The main part of the uterus is called the **body,** and the narrower part, the **cervix** (SER-viks; neck), is directed inferiorly. Internally, the **uterine cavity** in the fundus and uterine body continues through the cervix as the **cervical canal,** which opens into the vagina. The cervical canal is lined by mucous glands.

The uterine wall is composed of three layers: (1) an outer serous layer, called the perimetrium, (2) a middle, muscular layer called the myometrium, and (3) an inner layer called the endometrium (see figure 19.9). The **perimetrium** (per-ih-MEE-tree-um), or *serous layer,* of the uterus is formed from visceral peritoneum. The **myometrium** (my-oh-MEE-tree-um), or *muscular layer,* consists of smooth muscle, is quite thick, and accounts for the bulk of the uterine wall. The **endometrium** (en-doh-MEE-tree-um)

consists of simple columnar epithelial cells with an underlying connective tissue layer. Simple tubular glands, called spiral glands, are formed by folds of the endometrium. The superficial part of the endometrium is sloughed off during menstruation.

The uterus is supported by the broad ligament and the **round ligament.** In addition to these ligaments, much support is provided inferiorly to the uterus by skeletal muscles of the pelvic floor. If ligaments that support the uterus or muscles of the pelvic floor are weakened, as may occur due to childbirth, the uterus can extend inferiorly into the vagina, a condition called a **prolapsed uterus.** Severe cases require surgical correction.

Vagina

The **vagina** (vah-JIE-nah) is the female organ of copulation; it receives the penis during intercourse. It also allows menstrual flow and childbirth. The vagina extends from the uterus to the outside of the body (see figures 19.8 and 19.9). The superior portion of the vagina is attached to the sides of the cervix, so that a part of the cervix extends into the vagina.

The wall of the vagina consists of an outer muscular layer and an inner mucous membrane. The muscular layer is smooth muscle and contains many elastic fibers. Thus, the vagina can increase in size to accommodate the penis during intercourse, and it can stretch greatly during childbirth. The mucous membrane is moist stratified squamous epithelium that forms a protective surface layer. Lubricating fluid passes through the vaginal epithelium into the vagina.

In young females, the vaginal opening is covered by a thin mucous membrane called the **hymen** (HIGH-men; membrane). In rare cases, the hymen may completely close the vaginal orifice and it must be removed to allow menstrual flow. More commonly, the hymen is perforated by one or several holes. The openings in the hymen are usually greatly enlarged during the first sexual intercourse. The hymen can also be perforated or torn earlier in a young female's life during a variety of activities, including strenuous exercise. The condition of the hymen is therefore an unreliable indicator of virginity.

External Genitalia

The external female genitalia, also called the **vulva** (VUL-vah) or *pudendum* (pu-DEN-dum), consist of the vestibule and its surrounding structures (figure

19.12). The **vestibule** (VES-tih-byul) is the space into which both the vagina and the urethra open. The urethra opens into the vestibule just anterior to the vagina. The vestibule is bordered by a pair of thin, longitudinal skin folds called the **labia minora** (LAY-bee-ah, lips; my-NOH-rah, small). A small, erectile structure called the **clitoris** (KLIT-oh-ris) is located in the anterior margin of the vestibule. The two labia minora unite over the clitoris to form a fold of skin called the **prepuce.** Like the glans penis, the clitoris is well supplied with sensory receptors, and it is made up of erectile tissue (see figure 19.8).

On each side of the vestibule, between the vaginal opening and the labia minora, are openings of the **greater vestibular glands.** These glands produce a lubricating fluid that helps maintain the moistness of the vestibule.

Lateral to the labia minora are two prominent, rounded folds of skin called the **labia majora** (mah-JOH-rah; large). The two labia majora unite anteriorly at an elevation of tissue over the pubic symphysis called the **mons pubis** (MONZ PYU-bis) (figure 19.12). The lateral surfaces of the labia majora and the surface of the mons pubis are covered with coarse hair. The medial surfaces of the labia majora are covered with numerous sebaceous and sweat glands. The space between the labia majora is called the **pudendal cleft.** Most of the time, the labia majora are in contact with each other across the midline, closing the pudendal cleft and covering the deeper structures within the vestibule.

Figure 19.12 APR **Female External Genitalia**
Two folds of skin protect the vagina.

The **clinical perineum** (PER-ih-NEE-um; area between the thighs) is the region between the vagina and the anus. The skin and muscle of this region can tear during childbirth. Historically, to prevent such tearing, an incision called an **episiotomy** (eh-peez-ee-OT-oh-mee) is sometimes made in the clinical perineum. However, several medical associations have released statements that recommend against performing an episiotomy. Research has indicated there is no benefit to the mother or the child in most cases.

Mammary Glands

The **mammary** (MAM-ah-ree; relating to breasts) **glands** are the organs of milk production and are located in the **breasts** (figure 19.13). The mammary glands are modified sweat glands. Externally, each of the breasts of both males and females has a raised **nipple** surrounded by a circular, pigmented area called the **areola** (ah-REE-oh-luh).

Figure 19.13 APR **Anatomy of the Breast**

(*a*) Each lactiferous duct of the mammary gland branches. At the end of each branch is one or more alveoli. (*b*) The nonlactating breast has a duct system that is not extensively developed. The branches of the lactiferous ducts end as small, tubelike structures. (*c*) The lactating breast has a well-developed duct system with many branches. The branches of the lactiferous duct end with well-developed alveoli. Adipose tissue is abundant in both the nonlactating and the lactating breast.

In prepubescent children, the general structure of the male and female breasts is similar, and both males and females possess a rudimentary duct system. The female breasts begin to enlarge during puberty, under the influence of estrogen and progesterone. Some males also experience a minor and temporary enlargement of the breasts at puberty. Occasionally, the breasts of a male can become permanently enlarged, a condition called **gynecomastia** (GUY-nih-koh-MAS-tee-ah). Causes of gynecomastia include hormonal imbalances and the abuse of anabolic steroids.

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CLINICAL IMPACT

Cancer of the Breast

Cancer of the breast is a serious, often fatal disease that most often occurs in females. Regular self-examination of the breast can lead to early detection of breast cancer and effective treatment. In addition, **mammography** (mah-MOG-rah-fee) often allows tumors to be identified even before they can be detected by palpation. Mammography uses low-intensity x-rays to detect tumors in the soft tissue of the breast. Once a tumor is identified, a biopsy is normally performed to determine whether the tumor is benign or malignant. Most tumors of the mammary glands are benign, but those that are malignant can spread to other areas of the body and ultimately lead to death.

Each adult female breast contains mammary glands consisting of usually 15–20 glandular **lobes** covered by adipose tissue (figure 19.13*a,b*). It is primarily this superficial adipose tissue that gives the breast its form. Each lobe possesses a single **lactiferous duct** that opens independently to the surface of the nipple. The duct of each lobe is formed as several smaller ducts, which originate from **lobules,** converge. Within a lobule, the ducts branch and become even smaller. In the milk-producing, or lactating, mammary gland, the ends of these small ducts expand to form secretory sacs called **alveoli. Myoepithelial cells** surround the alveoli and contract to expel milk from the alveoli (figure 19.13*c*).

The breasts are supported by suspensory ligaments that extend from the fascia over the pectoralis major muscles to the skin over the breasts (figure

19.13*b*).

The nipples are very sensitive to tactile stimulation and contain smooth muscle cells that contract, causing the nipple to become erect in response to stimulation. These smooth muscle cells respond to stimuli, such as touch, cold, and sexual arousal.

19.6 PHYSIOLOGY OF FEMALE REPRODUCTION

Learning Outcomes *After reading this section, you should be able to*

A. Describe the changes that occur in females during puberty.
B. Describe the changes in the ovary and uterus that occur during the menstrual cycle.
C. List the hormones of the female reproductive system, and explain how their secretion is regulated.
D. Explain the events that occur during the female sexual act.
E. Define menopause, and describe the changes that result from it.

Female reproduction is controlled by both hormonal and nervous system mechanisms.

Puberty in Females

The initial change that results in puberty is most likely maturation of the hypothalamus. In females, puberty, which typically begins between ages 11 and 13 and is largely completed by age 16, is marked by the first episode of menstrual bleeding, which is called **menarche** (me-NAR-key; *mēn,* month + *archē,* beginning). During puberty, the vagina, uterus, uterine tubes, and external genitalia begin to enlarge. Adipose tissue is deposited in the breasts and around the hips, causing them to enlarge and assume an adult form. In addition, pubic and axillary hair grows. The development of sexual drive is also associated with puberty.

Before puberty, the rate of GnRH secretion from the hypothalamus and the rate of LH and FSH secretion from the anterior pituitary are very low. Estrogen and progesterone from the ovaries have a strong negative-feedback effect on the hypothalamus and pituitary.

After the onset of puberty, the hypothalamus and anterior pituitary secrete larger amounts of GnRH, LH, and FSH. Estrogen and progesterone have less of a negative-feedback effect on the hypothalamus and pituitary, and a sustained increase in estrogen concentration has a positive-feedback effect.

The normal cyclical pattern of reproductive hormone secretion that occurs during the menstrual cycle becomes established.

Menstrual Cycle

The term **menstrual** (MEN-stru-al) **cycle** refers to the series of changes that occur in sexually mature, nonpregnant females and that result in menses. **Menses** (MEN-seez; month) is a period of mild hemorrhage, during which part of the endometrium is sloughed and expelled from the uterus. In discussing the menstrual cycle, we normally describe it as being about 28 days long, although it can be as short as 18 days in some females or as long as 40 days in others. Variation in duration of the menstrual cycle occurs among females, but can also occur from month to month in the same female, depending on many factors, including nutrition, stress, and level of activity (figure 19.14 and table 19.3). The menstrual cycle results from the cyclical changes that occur in the endometrium of the uterus. These changes, in turn, result from the cyclical changes that occur in the ovary and are controlled by the secretions of FSH and LH from the anterior pituitary gland. In this textbook, we will discuss the menstrual cycle in terms of changes in the uterus and relate those changes to development of the oocyte and follicle in the ovary.

Figure 19.14 APR **Menstrual Cycle**

Over approximately 30 days, fluctuations occur in the levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion from the anterior pituitary gland and in the levels of estrogen and progesterone secretion from the ovary. In addition, changes in the ovary and changes in the endometrium of the uterus are correlated with the changes in hormone secretion throughout the menstrual cycle. Ovulation occurs on about day 14.

Table 19.3	Events During the Menstrual Cycle
Menses (day 1 to day 4 or 5 of the menstrual cycle)	
Pituitary	The rate of FSH and LH secretion is low, but the rate of FSH secretion

gland	increases as progesterone levels decline.
Ovary	The rate of estrogen and progesterone secretion is low after degeneration of the corpus luteum produced during the previous menstrual cycle.
Uterus	In response to declining progesterone levels, the endometrial lining of the uterus sloughs off, resulting in menses followed by repair of the endometrium.
Proliferative Phase (from day 4 or 5 until ovulation on about day 14)	
Pituitary gland	The rate of FSH and LH secretion is only slightly elevated during most of the proliferative phase; FSH and LH secretions increase near the end of the proliferative phase in response to increasing estrogen secretion from the ovaries.
Ovary	Developing follicles secrete increasing amounts of estrogen, especially near the end of the proliferative phase; increasing FSH and LH cause additional estrogen secretion from the ovaries near the end of the proliferative phase.
Uterus	Estrogen causes endometrial cells of the uterus to divide. The endometrium of the uterus thickens, and tubelike glands form. Estrogen causes the cells of the uterus to be more sensitive to progesterone by increasing the number of progesterone receptors in uterine tissues.
Ovulation (about day 14)	
Pituitary gland	The rate of FSH and LH secretion increases rapidly just before ovulation in response to increasing estrogen levels. Increasing FSH and LH levels stimulate estrogen secretion, resulting in a positive-feedback cycle.
Ovary	LH causes final maturation of a mature follicle and initiates the process of ovulation. FSH acts on immature follicles and causes several of them to begin to enlarge.
Uterus	The endometrium continues to divide in response to estrogen.
Secretory Phase (from about day 14 to day 28)	
Pituitary gland	Estrogen and progesterone reach levels high enough to inhibit FSH and LH secretion from the pituitary gland.
Ovary	After ovulation, the follicle is converted to the corpus luteum; the corpus luteum secretes large amounts of progesterone and smaller amounts of estrogen from shortly after ovulation until about day 24 or 25. If fertilization does not occur, the corpus luteum degenerates after about day 25, and the rate of progesterone secretion rapidly declines to low levels.
Uterus	In response to progesterone, the endometrial cells enlarge, the endometrial layer thickens, and the glands of the endometrium reach their greatest degree of development; the endometrial cells secrete a small amount of fluid. After progesterone levels decline, the endometrium begins to degenerate.
Menses (day 1 to day 4 or 5 of the next menstrual cycle)	
Pituitary gland	The rate of LH remains low, and the rate of FSH secretion increases as progesterone levels decline.

Ovary	The rate of estrogen and progesterone secretion is low.
Uterus	In response to declining progesterone levels, the endometrial lining of the uterus sloughs off, resulting in menses followed by repair of the endometrium.

Menses

In a menstrual cycle in which pregnancy does not occur, the levels of estrogen and progesterone decline to very low levels as the corpus luteum degenerates. The drop in these hormones initiates the beginning of menses, or menstrual bleeding. Day 1 of the menstrual cycle is when the endometrium begins to slough off. Menses typically lasts 4 or 5 days and can be accompanied by strong uterine contractions, called menstrual cramps, that are extremely uncomfortable in some females. Menstrual cramps are the result of forceful myometrial contractions that occur before and during menstruation. The cramps can result from excessive secretion of prostaglandins. As the endometrium of the uterus sloughs off, it becomes inflamed, and prostaglandins are produced as part of the inflammation. Many individuals can alleviate painful cramps by taking medications, such as aspirin-like drugs, that inhibit prostaglandin biosynthesis just before the onset of menstruation. These medications, however, are not effective in treating all painful menstruation, especially when the cause of the pain, such as that experienced by females who have tumors of the myometrium, is not due to the inflammatory response.

Proliferative Phase

The time between the end of menses and ovulation is called the **proliferative phase.** During the proliferative phase, the endometrium begins to regenerate. Meanwhile, in the ovary, the secondary follicles mature; as they do so, they secrete increasing amounts of estrogen. Estrogen acts on the uterus and causes the epithelial cells of the endometrium to divide rapidly. The endometrium thickens, and spiral glands form.

Ovulation occurs during the proliferative phase on about day 14 of the menstrual cycle. After ovulation, the secretory phase of the menstrual cycle is initiated. The sustained increase of estrogen secreted by the developing follicles stimulates GnRH secretion from the hypothalamus. GnRH, in turn, triggers FSH and LH secretion from the anterior pituitary gland. FSH stimulates estrogen secretion at an increasing rate from the developing follicles. This positive-feedback loop produces a series of larger and larger surges of FSH and LH secretion. Ovulation occurs in response to the large increases in LH levels that normally occur on about day 14 of the menstrual cycle. This large increase in LH is also responsible for the development of the

corpus luteum. As described earlier, although the timing of ovulation varies from individual to individual, it can also vary within an individual from one menstrual cycle to the next. To avoid or optimize contraception, it is critical to predict ovulation; however, there is no single reliable method that can predict its exact timing. The simplest method of predicting ovulation is looking for a drop in basal body temperature preceding ovulation, but it is the least reliable method. Ovulation predictor tests that measure the peak in LH can be purchased over the counter in many stores.

Following ovulation, the corpus luteum begins to secrete greater amounts of progesterone. Progesterone acts on the uterus, causing the cells of the endometrium to become larger and to secrete a small amount of fluid. Insufficient levels of progesterone from the corpus luteum could result in the spontaneous loss of a pregnancy. Fortunately, if caught early enough, progesterone supplements can be used to help maintain the pregnancy. Together, progesterone and estrogen act on the hypothalamus and anterior pituitary gland to inhibit GnRH, LH, and FSH secretion. Thus, LH and FSH levels decline after ovulation.

Secretory Phase

The period after ovulation and before the next menses is the **secretory phase** of the menstrual cycle, called this because of the small amount of fluid secreted by the cells of the endometrium. During the secretory phase, the lining of the uterus reaches its greatest degree of development.

CLINICAL IMPACT

Amenorrhea

The absence of a menstrual cycle is called **amenorrhea** (ah-men-oh-REE-ah; without menses). If the pituitary gland does not function properly because of abnormal development, a female does not begin to menstruate at puberty. This condition is called **primary amenorrhea.** In contrast, if a female has had normal menstrual cycles and later stops menstruating, the condition is called **secondary amenorrhea.** One cause of secondary amenorrhea is anorexia, in which a lack of food causes the hypothalamus of

the brain to decrease GnRH secretion to levels so low that the menstrual cycle cannot occur. Many female athletes and ballet dancers who have rigorous training schedules have secondary amenorrhea. The physical stress that can be coupled with inadequate food intake also results in very low GnRH secretion. Increased food intake for anorexic females or reduced training for dancers and athletes generally restores normal hormone secretion and normal menstrual cycles.

Secondary amenorrhea can also be the result of a pituitary tumor that decreases FSH and LH secretion or a lack of GnRH secretion from the hypothalamus due to head trauma or a tumor.

In addition, secondary amenorrhea can occur due to a lack of normal hormone secretion from the ovaries, which can result from autoimmune diseases that attack the ovary or occur due to **polycystic ovarian disease,** in which cysts in the ovary produce large amounts of androgen, which is converted to estrogen by other body tissues. The increased estrogen prevents the normal cycle of FSH and LH secretion required for ovulation to occur. Other hormone-secreting tumors of the ovary can also disrupt the normal menstrual cycle and result in amenorrhea.

Endometriosis (EN-doh-mee-tree-OH-sis) is a condition in which endometrial tissue migrates from the lining of the uterus into the peritoneal cavity, where it attaches to the surface of organs. Common sites of attachment are the ovaries and the pelvic peritoneum. Other possible sites are the intestines, uterus, urinary bladder, and vagina. If the attached endometrial tissue has an adequate blood supply, it proliferates, breaks down, and bleeds in response to the hormones produced during the menstrual cycle. Unlike the normal endometrium, which is shed each month during menstruation, endometrial tissue attached outside of the uterus causes lesions or tumors to develop, resulting in internal bleeding, scar tissue formation, inflammation, and pain. Other major complications of endometriosis are infertility and ovarian cyst formation. Up to 40% or 50% of infertile females have endometriosis.

If fertilization occurs, the zygote undergoes several cell divisions to produce a collection of cells called the **blastocyst** (BLAS-toh-sist). The blastocyst passes through the uterine tube and arrives in the uterus by 7 or 8 days after ovulation. The endometrium is prepared to receive the blastocyst, which becomes implanted in the endometrium, where it continues to develop.

If the secondary oocyte is not fertilized, the endometrium sloughs away as a result of declining blood progesterone levels. Without human chorionic gonadotropin from a zygote, the corpus luteum begins to produce less progesterone by day 24 or 25 of the menstrual cycle. By day 28, the declining progesterone causes the endometrium to slough away to begin menses and the next menstrual cycle. The declining progesterone secretion results in a

small increase in FSH secretion at the beginning of the next menses, which triggers more follicles to mature.

Apply It 4

Explain the effect of administering a relatively large amount of progesterone and estrogen just before the increase in LH that precedes ovulation.

An **ectopic pregnancy** results if implantation occurs anywhere other than in the uterine cavity. The most common site of ectopic pregnancy is the uterine tube. Implantation in the uterine tube is eventually fatal to the fetus and can cause the tube to rupture. In some rare cases, implantation occurs in the mesenteries of the abdominal cavity; the fetus can develop normally but must be delivered by cesarean section. However, maternal mortality rates for abdominal pregnancies are significantly higher than for uterine tube ectopic pregnancies.

Menopause

When a female is 40–50 years old, the menstrual cycles become less regular, and ovulation does not occur consistently during each cycle. Eventually, the cycles stop completely. The cessation of menstrual cycles is called **menopause** (MEN-oh-paws; *mēn,* month + *pausis,* cessation), and the whole time period from the onset of irregular cycles to their complete cessation is called the female **climacteric** (KLI-mak-ter-ik).

The major cause of menopause is age-related changes in the ovaries. The number of follicles remaining in the ovaries of menopausal females is small. In addition, the follicles that remain become less sensitive to stimulation by FSH and LH, and therefore fewer mature follicles and corpora lutea are produced.

Older females experience gradual changes in response to the reduced amount of estrogen and progesterone produced by the ovaries (table 19.4). For example, during the climacteric, some females experience sudden episodes of uncomfortable sweating (hot flashes), fatigue, anxiety, temporary decrease in libido, and occasionally emotional disturbances. Many of these symptoms can be treated successfully with hormone replacement therapy (HRT), which usually consists of small amounts of estrogen and progesterone. HRT has been linked to a slightly increased risk of developing breast cancer, uterine cancer, heart attack, stroke, or blood clots. On the positive side, HRT slows the decrease in bone density that can become severe

in some females after menopause, and it decreases the risk of developing colorectal cancer.

Table 19.4 Possible Changes in Postmenopausal Females Caused by Decreased Ovarian Hormone Secretion

	Changes
Menstrual cycle	Five to seven years before menopause, the cycle becomes irregular; the number of cycles in which ovulation does not occur and in which corpora lutea do not develop increases.
Uterus	Gradual increase in irregular menstruations is followed by no menstruation; the endometrium finally atrophies, and the uterus becomes smaller.
Vagina and external genitalia	The epithelial lining becomes thinner; the external genitalia become thinner and less elastic; the labia majora become smaller; the pubic hair decreases; reduced secretion leads to dryness; the vagina is more easily inflamed and infected.
Skin	The epidermis becomes thinner.
Cardiovascular system	Hypertension and atherosclerosis occur more frequently.
Vasomotor instability	Hot flashes and increased sweating are correlated with vasodilation of cutaneous blood vessels; the hot flashes are related to decreased estrogen levels.
Libido	Temporary changes, usually a decrease in libido, are associated with the onset of menopause.
Fertility	Fertility begins to decline about 10 years before the onset of menopause; by age 50, almost all the oocytes and follicles have degenerated.
Pituitary function	Low levels of estrogen and progesterone produced by the ovaries cause the pituitary gland to secrete larger than normal amounts of LH and FSH; increased levels of these hormones have little effect on the postmenopausal ovaries.

Female Sexual Behavior and the Female Sex Act

Sexual drive in females, like sexual drive in males, is dependent on hormones. Testosterone-like hormones, and possibly estrogen, affect brain cells (especially in the area of the hypothalamus) and influence sexual behavior. Testosterone-like hormones are produced primarily in the adrenal cortex. Psychological factors also play a role in sexual behavior. The sensory and motor neural pathways involved in controlling female sexual responses are similar to those found in the male.

During sexual excitement, erectile tissue within the clitoris and around the vaginal opening becomes engorged with blood. The mucous glands within the vestibule, especially the greater vestibular glands, secrete small amounts of mucus. Larger amounts of mucuslike fluid are also extruded into the vagina through its wall. The mucus provides lubrication to allow easy entry and movement of the penis in the vagina during intercourse. Stimulation of the female's genitals during sexual intercourse and psychological stimuli normally trigger an **orgasm,** or *climax*. The vaginal and uterine smooth muscle, as well as the surrounding skeletal muscles, contract rhythmically, and muscle tension increases throughout much of the body. After the sex act, there is a period of **resolution,** which is characterized by an overall sense of satisfaction and relaxation. In contrast to males, females can be receptive to further stimulation and can experience successive orgasms. Although orgasm is a pleasurable component of sexual intercourse, it is not necessary for females to experience an orgasm for fertilization to occur.

Control of Pregnancy

Birth control methods, also called *contraception methods,* are procedures or devices used to prevent pregnancy (table 19.5). In addition, protection from sexually transmitted infections (STIs, table 19.6) can be achieved with some birth control methods. There are six main types of birth control. They are listed in order from the most effective methods to the least effective methods: (1) long-acting reversible contraception, (2) sterilization, (3) hormonal methods, (4) barrier methods, (5) fertility awareness, and (6) emergency contraception. For each of these methods, there are measures of effectiveness for perfect use each time compared with typical use. We express the effectiveness of a particular birth control method as the number out of every 100 females who could become unintentionally pregnant with typical use within the first year of beginning a particular method. We present a few examples of each type of birth control rather than an exhaustive list of all birth control methods that are available.

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TABLE 19.5 Methods of Birth Control

Birth Control Method		Effectiveness (number of females in 100 who became unintentionally pregnant with typical use)
Long-acting reversible contraception		
IUD		<1
Birth control implant		<1
Permanent Methods		
Female		<1
Male		<1
Hormonal Methods		

Birth Control Method		Effectiveness (number of females in 100 who became unintentionally pregnant with typical use)
Injectables	Injectable	6
Pills	Martin Shields / Alamy stock photo	9
Patch and vaginal ring	Patch Ring	9
Barrier Methods		
Female condom	Female condom	21

Birth Control Method		Effectiveness (number of females in 100 who became unintentionally pregnant with typical use)
Male condom	Male condom	18
Diaphragm	Jill Braaten/McGraw-Hill Education	12
Fertility-Awareness—Based Methods		
Standard and 2-day method	Alexey Boldin/Shutterstock	12-14
Symptothermal	D. Hurst/Alamy Stock Photo	2

Long-Acting Reversible Contraception

This type of birth control provides the highest rates of effectiveness with typical use. In addition, these methods do not require daily action or action

with each incidence of sexual intercourse. However, none of these listed methods reduce the risk of STIs.

1. *Intrauterine devices.* An **intrauterine device (IUD)** is a medical device that is placed in a female's uterus through the cervix by a medical caregiver. There are two main types of IUDs: (a) a copper IUD and (b) a synthetic progesterone-coated or levonorgestrel-releasing (LNG-IUD). Copper IUDs are effective for up to 10 years, while the LNG-IUDs are effective for approximately 5 years. Both types of IUDs work primarily by preventing fertilization through thickening of cervical mucus. The thicker mucus prevents sperm cells from entering the uterus. In addition, the copper from the copper IUDs damages sperm cells. Both types of IUDs result in less than 1 unintended pregnancy/100 females.
2. *Birth control implant.* The **implant** is a small capsule containing etonogestrel, or synthetic progesterone, that a female's medical caregiver places under the skin of the upper arm. It slowly releases hormone for a period of 3–5 years. The hormone acts to thicken the cervical mucus, which prevents sperm cells from entering the uterus; the hormone also prevents ovulation. The implant results in less than 1 unintended pregnancy/100 females.

Permanent Methods of Birth Control

A male or female may choose a surgical sterilization method as a form of permanent birth control. None of these listed methods reduce the risk of STIs.

1. *Female sterilization.* In females, the most common permanent birth control is **tubal ligation** where the uterine tubes are blocked or cut. The cutting or blocking of the uterine tubes prevents the oocyte and sperm cell from meeting, and thus prevents fertilization. Tubal ligations result in less than 1 unintended pregnancy/100 females.
2. *Male sterilization.* The permanent form of birth control in males is a **vasectomy** where the ductus (vas) deferens is cut or blocked. A vasectomy prevents sperm cells from being ejaculated as part of the semen. Thus, no sperm cells enter the vagina. Three months after surgery, a vasectomy results in less than 1 unintended pregnancy/100 females.

Hormonal Methods of Birth Control

The principal mechanism of hormonal birth control methods is prevention of ovulation. Development of male hormonal birth control to inhibit sperm cell production is under investigation and is not widely available. Some of these methods require daily attention and none of these reduce the risk of STIs.

1. *Injectables.* These hormonal methods must be injected under the skin every 2–3 months for progesterone-only injectables and into the muscle every month for combined injectable contraceptives. The progesterone-only injectable acts to thicken cervical mucus to prevent sperm cell entry into the uterus as well as preventing ovulation. The combined injectables prevent ovulation. Injectables result in about 6 unintended pregnancies/100 females. The challenge with injectables is being sure to receive repeat injections within the proper time frame.
2. *Pills.* Oral contraceptives are taken almost exclusively by females since male oral contraceptives are not currently available. One form, referred to as "the pill," is a combination of estrogen and progestogen (synthetic progesterone) and works to prevent ovulation. Another form, "the minipill," contains only progestogen and works to thicken cervical mucus. Each of these pills results in about 9 unintended pregnancies/100 females. The challenge with the pills is remembering to take a pill each day.

3. *Patch and vaginal ring.* Each of these methods continuously releases progestogen and estrogen for 3 weeks and then a new one is put into place. The transdermal contraceptive patch, also simply called the patch, is applied directly to the skin every 3 weeks. The vaginal ring is inserted into the vagina and remains in place for 3 weeks and is then removed. A new ring is inserted after 1 week. Each of these methods prevents ovulation and results in about 9 unintended pregnancies/100 females. The challenge is to remember to change the patch or ring on the appropriate schedule.

Barrier Methods of Birth Control

A barrier method is a device that physically prevents the sperm cells and oocyte from meeting. The major advantage of certain barrier methods is that these are the only contraceptive methods that also reduce the risk of STI transmission. To reduce the risk of STIs, the Centers for Disease Control and Prevention (CDC) recommend that condoms should always be used.

1. *Female condom.* A female condom is made of thin, soft plastic, which fits inside the female's vagina. The condom traps any sperm cells released into the vagina and prevents them from reaching the oocyte. It also protects against HIV and other STIs. Use of the female condom results in about 21 unintended pregnancies/100 females. The challenge with the female condom is that it must be inserted before each incidence of sexual intercourse.
2. *Male condom.* A male condom is a covering that is placed over a male's erect penis. Condoms can be made of several different materials, including natural

latex, Vytex©, which has been treated to remove 90% of proteins responsible for latex allergies, or synthetic latex, called polyisoprene. There are also completely nonlatex condoms made of polyurethane, and "lambskin" condoms, which are made of sheep intestine. However, the latter have not been shown to reduce the risk of STIs. All other condoms reduce the risk of HIV transmission and many other STIs. Use of male condoms results in approximately 18 unintended pregnancies/100 females. The challenge is to use them correctly with every instance of intercourse.

3. *Diaphragm.* A diaphragm is a flexible latex dome that a female inserts into her vagina along with a spermicide before each instance of sexual intercourse. The diaphragm will unfold and fit over the cervix to block sperm cells from entering the uterus. However, unlike the other barrier methods, such as the male and female condoms, a diaphragm does not prevent transmission of STIs. In addition, a diaphragm must be refitted in the event of a significant (20%) weight gain or loss. A diaphragm results in about 12 unintended pregnancies/100 females.

Fertility-Awareness–Based Methods of Birth Control

With fertility-awareness–based methods, a female determines and tracks the days when she is most fertile. In each menstrual cycle, there is approximately a 6–8 day window during which a female has the greatest chance of becoming pregnant if she has unprotected intercourse. This window is due to the fact that both the oocyte and sperm cell are viable for a period of time inside the female reproductive tract. Sperm cells are able to survive up to 5 days inside the female. The oocyte is viable for up to 24 hours after ovulation. Thus, fertility-awareness–based methods require focused attention. It is estimated that only 25–30% of females know when their most fertile period occurs.

1. *Standard days method.* A female tracks her fertile period using a tracking tool such as cycle beads, or an app for her smartphone. This method is effective for females whose cycles are 26–32 days long. Using this method, around 12 in 100 females experienced an unintended pregnancy.
2. *Two-day method.* Females monitor their cervical mucus traits such as color and consistency. Around 14 in 100 females become unintentionally pregnant using this method. When cervical mucus monitoring is combined with body temperature tracking, this method is called the symptothermal method and results in only 2 in 100 females becoming unintentionally pregnant.

Emergency Contraception

If unprotected intercourse occurs, ingestion of emergency contraceptive pills or insertion of a copper IUD significantly lowers the possibility of an unintended pregnancy. Both methods must be utilized within 5 days after unprotected intercourse. Emergency contraceptive pills such as Plan B (the morning-after pill) or Ella (the week-after pill) disrupt or delay ovulation. The copper IUD works to immobilize sperm cells preventing them from reaching the oocyte. It also causes thinning of the endometrium and potentially inhibits the ability of oocytes to be fertilized. These methods result in only 1 in 100 unintended pregnancies.

Traditional Methods of Birth Control

Some traditional birth control methods are still in use; however, only abstinence is 100% effective in prevention of unintended pregnancies. Other traditional methods include the withdrawal method where the male ejaculates outside the female's body, and the calendar method, or rhythm method, where fertile days are estimated. Each of these traditional methods results in approximately 15–17 in 100 females becoming unintentionally pregnant.

Infertility in Females

Causes of infertility in females include malfunctions of the uterine tubes, reduced hormone secretion from the pituitary gland or the ovaries, and interruption of implantation. Uterine tube malfunction can occur when infections result in pelvic inflammatory disease (PID), which causes adhesions to form in one or both of the uterine tubes. Inadequate secretion of LH and FSH can occur for a variety of reasons, including hypothyroidism or a tumor in or trauma to the hypothalamus or anterior pituitary. Decreased secretion of LH and FSH interrupts ovulation.

Interruption of implantation can result from uterine tumors or conditions causing abnormal ovarian hormone secretion. For example, premature degeneration of the corpus luteum causes progesterone levels to decline and menses to occur. If the corpus luteum degenerates before the placenta begins to secrete progesterone, the endometrium and the developing embryonic mass will degenerate and be eliminated from the uterus. The conditions that result in secondary amenorrhea also reduce fertility.

EFFECTS OF AGING ON THE REPRODUCTIVE SYSTEM

Aging affects the reproductive system in both males and females in several ways. Sexual activity is often maintained in males and females as they age, but the frequency of sexual intercourse usually decreases gradually.

In males, benign prostatic enlargement is common after 50 years of age. A major consequence of prostatic enlargement is blockage of the prostatic urethra. Treatments for benign prostate enlargement can reverse its negative effects. In addition, the frequency of prostate cancer increases as males age and is a significant cause of death in males. In addition, the tendency for erectile dysfunction increases as men age. However, less than 15% of males age 60 or under experience abnormal erectile dysfunction. Keeping physically healthy can minimize some factors leading to abnormal erectile dysfunction, and medical treatments are available.

In females, the most significant age-related change is menopause. By age 50, the amount of estrogen and progesterone produced by the ovaries has decreased. The uterus decreases in size, and the endometrium decreases in thickness. The times between menses become irregular and longer until menstruation stops. The vaginal wall becomes thinner and less elastic, and there is less lubricant in the vagina, resulting in an increased tendency for vaginal yeast infections. However, wearing cotton underwear and loose clothing reduces this possibility. In the event of infections, very effective medical treatments are available.

Approximately 10% of all females will develop breast cancer. The incidence of breast cancer is greatest between 45 and 65 years of age and is greater for females who have a family history of breast cancer. The single most important measure to guard against death from breast cancer is early detection through breast self-exams and yearly mammograms after age 40. The incidences of uterine cancer, ovarian cancer, and cervical cancer all increase between 50 and 65 years of age. Annual medical checkups, including Pap smears for cervical cancer, are important in order to detect cancer at early stages, when it can be easily treated.

Benign Uterine Tumors

Background Information

Molly had four children and was 43. She noticed that menstruation was gradually becoming more severe and lasting up to several days longer each time. After menstruating almost continuously for 2 months, Molly made an appointment with her physician. Palpation of the uterus indicated the presence of enlarged masses in Molly's uterus. The doctor performed a D&C, which is dilation of the cervix and scraping (curettage) of the endometrium to remove growths or other abnormal tissues. The results of the D&C indicated that Molly had developed leiomyomas. **Leiomyomas** (LIE-oh-my-OH-maz), also called uterine fibroids, are fibroid tumors of the uterus. They are one of the most common disorders of the uterus, and the most frequent tumor in females, affecting one of every four. However, three-fourths of the females with this condition experience no symptoms (figure 19.15). The enlarged masses that originate from smooth muscle tissue compress the uterine lining (endometrium), resulting in ischemia and inflammation (figure 19.16). The increased inflammation, which shares some characteristics with menstruation, results in frequent and severe menses, with associated abdominal cramping due to strong uterine contractions. Constant menstruation is a frequent manifestation of these tumors, and it is one of the most common reasons females select to have the uterus removed, a procedure called a **hysterectomy** (his-ter-EK-toh-mee).

Figure 19.15 APR **Effects of Benign Uterine Tumors on the Body's Organ Systems**
A benign uterine tumor can affect many of the body's systems, as this diagram illustrates.

Figure 19.16 **Benign Uterine Tumors**
Leiomyomas, or fibroid tumors, are enlarged masses of smooth muscle. They are located near the mucosa (submucous), within the myometrium (interstitial), or near the serosa (subserous).

Table 19.6 REPRESENTATIVE DISEASES AND DISORDERS: Reproductive System	
Condition	**Description**

Condition	Description
Infectious Diseases	
Pelvic inflammatory disease (PID)	Bacterial infection of the female pelvic organs; commonly caused by a vaginal or uterine infection with the bacteria gonorrhea or chlamydia; early symptoms include increased vaginal discharge and pelvic pain; antibiotics are effective; if untreated, can lead to sterility or be life-threatening
Sexually Transmitted Infections	Commonly known as STIs; spread by intimate sexual contact
Nongonococcal urethritis (non-GON-oh-kok-al you-ree-THRY-tis)	Inflammation of the urethra that is not caused by gonorrhea; can be caused by trauma, insertion of a nonsterile catheter, or sexual contact; usually due to infection with the bacterium *Chlamydia trachomatis* (klah-MI-dee-ah trah-KO-mah-tis); may go unnoticed and result in pelvic inflammatory disease or sterility; antibiotics are effective treatment
Trichomoniasis (TRIK-oh-moh-NYE-ah-sis)	Caused by *Trichomonas* (TRIK-oh-MOH-nas), a protozoan commonly found in the vagina of females and in the urethra of males; results in a greenish-yellow discharge with a foul odor; more common in females than in males
Gonorrhea (gon-oh- REE-ah)	Caused by the bacterium *Neisseria gonorrhoeae* (nye-SEE-ree-ah gon-oh-REE-ah), which attaches to the epithelial cells of the vagina or male urethra and causes pus to form; pain and discharge from the penis occur in males; asymptomatic in females in the early stages; can lead to sterility in males and pelvic inflammatory disease in females
Genital herpes (HER-pees)	Caused by herpes simplex 2 virus; characterized by lesions on the genitals that progress into blisterlike areas, making urination, sitting, and walking painful; antiviral drugs can be effective
Genital warts	Caused by a viral infection; very contagious; warts vary from separate, small growths to large, cauliflower-like clusters; lesions are not painful, but sexual intercourse with lesions is; treatments include topical medicines and surgery to remove the lesions
Syphilis (SIF-ih-lis)	Caused by the bacterium *Treponema pallidum* (trep-oh-NEE-mah PAL-i-dum); can be spread by sexual contact; multiple disease stages occur; children born to infected mothers may be developmentally delayed; antibiotics are effective

Condition	Description
Acquired immunodeficiency syndrome (AIDS)	Caused by the human immunodeficiency virus (HIV), which ultimately destroys the immune system (see chapter 14); transmitted through intimate sexual contact or by allowing infected body fluids into the interior of another person

Apply It 5

When discussing her condition with her mother, Molly discovered that her mother had experienced frequent menses that were irregular and prolonged when she was in her late 40s. Molly's mother did not have a hysterectomy, and in a few years, the frequency gradually began to subside. Explain.

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SUMMAR Y

19.1 Functions of the Reproductive System

The reproductive system produces male and female gametes, enhances fertilization of an oocyte by a sperm, nurtures the new individual until birth (in the female), and produces reproductive hormones.

19.2 Formation of Gametes

The reproductive organs in males and females produce gametes by meiosis.

1. Two consecutive cell divisions halve the chromosome number from 46 total chromosomes to 23 total chromosomes.
2. Meiosis forms male and female gametes.

19.3 Male Reproductive System

Scrotum

1. The scrotum is a sac containing the testes.
2. The dartos and cremaster muscles help regulate testes temperature.

Testes

The testes are divided into lobules containing the seminiferous tubules and interstitial cells.

Spermatogenesis

1. Spermatogenesis begins in the seminiferous tubules at the time of puberty.
2. Sustentacular cells nourish the sperm cells and produce small amounts of hormones.
3. Spermatogonia divide (mitosis) to form primary spermatocytes.
4. Primary spermatocytes divide by meiosis to produce first secondary spermatocytes and then spermatids. The spermatids then mature to form sperm cells.
5. A spermatid develops a head, midpiece, and flagellum to become a sperm cell. The head contains the acrosome and the nucleus.

Ducts

1. The epididymis, a coiled tube system, is located on the testis and is the site of sperm maturation. Final changes, called capacitation of sperm cells, occur after ejaculation.
2. The seminiferous tubules lead to the rete testis, which opens into the efferent ductules that extend to the epididymis.
3. The ductus deferens passes from the epididymis into the abdominal cavity.
4. The ejaculatory duct is formed by the joining of the ductus deferens and the duct from the seminal vesicle.
5. The ejaculatory ducts join the prostatic urethra within the prostate gland.
6. The urethra extends from the urinary bladder through the penis to the outside of the body.

Penis

1. The penis consists of erectile tissue.
2. The two corpora cavernosa form the dorsum and the sides.

3. The corpus spongiosum forms the ventral portion and the glans penis, and it encloses the spongy urethra. The prepuce covers the glans penis.

Glands

1. The seminal vesicles empty into the ejaculatory duct.
2. The prostate gland consists of glandular and muscular tissue and empties into the urethra.
3. The bulbourethral glands empty into the urethra.

Secretions

1. Semen is a mixture of sperm cells and gland secretions.
2. The bulbourethral glands and the urethral mucous glands produce mucus that neutralizes the acidic pH of the urethra.
3. The testicular secretions contain sperm cells.
4. The seminal vesicle fluid contains nutrients, prostaglandins, and proteins that coagulate.
5. The prostate fluid contains nutrients and proteolytic enzymes, and it neutralizes the pH of the vagina.

19.4 Physiology of Male Reproduction

Regulation of Reproductive Hormone Secretion

1. GnRH is produced in the hypothalamus and released in surges.
2. GnRH stimulates release of LH and FSH from the anterior pituitary.
3. LH stimulates the interstitial cells to produce testosterone.
4. FSH binds to sustentacular cells and stimulates spermatogenesis and secretion of inhibin.
5. Testosterone has a negative-feedback effect on GnRH, LH, and FSH secretion.
6. Inhibin has a negative-feedback effect on FSH secretion.

Puberty in Males

1. Before puberty, small amounts of testosterone inhibit GnRH release.

2. During puberty, testosterone does not completely suppress GnRH release, resulting in increased production of FSH, LH, and testosterone.

Effects of Testosterone

1. Testosterone causes enlargement of the genitals and is necessary for spermatogenesis.
2. Testosterone is responsible for the development of secondary sexual characteristics.

Male Sexual Behavior and the Male Sex Act

1. Testosterone is required for normal sex drive.
2. Stimulation of the sex act can be tactile or psychological.
3. Sensory impulses pass to the sacral region of the spinal cord.
4. Motor stimulation causes erection, mucus production, emission, and ejaculation.

Infertility in Males

The most common cause of male infertility is a low sperm cell count.

19.5 Female Reproductive System

Ovaries, Oogenesis, Follicle Development, and Fertilization

1. By the fourth month of development, the ovaries contain 5 million oogonia.

2. By birth, many oogonia have degenerated, and for the remaining oogonia meiosis has stopped in prophase I, causing them to become primary oocytes.
3. By puberty, 300,000 to 400,000 primary oocytes remain, of which about 400 will be released from the ovaries.
4. Ovulation is the release of an oocyte from an ovary. The first meiotic division is completed, and a secondary oocyte is released.
5. A sperm cell penetrates the secondary oocyte, the second meiotic division is completed, and the nuclei of the oocyte and sperm cell are united to complete fertilization.
6. A primordial follicle is a primary oocyte surrounded by a single layer of flat granulosa cells.
7. In primary follicles, the oocyte enlarges, and granulosa cells become cuboidal and form more than one layer. A zona pellucida is present.

8. In a secondary follicle, fluid-filled vesicles appear, and a theca forms around the follicle.
9. In a mature follicle, vesicles fuse to form an antrum, and the primary oocyte is surrounded by cumulus cells.
10. During ovulation, the mature follicle ruptures, releasing the secondary oocyte, surrounded by cumulus cells, into the peritoneal cavity.
11. The remaining granulosa cells in the follicle develop into the corpus luteum.
12. If fertilization occurs, the corpus luteum persists. If there is no fertilization, it degenerates.

Uterine Tubes

1. The ovarian end of the uterine tube is surrounded by fimbriae.
2. Cilia on the fimbriae move the oocyte into the uterine tube.
3. Fertilization usually occurs in the ampulla of the uterine tube, which is near the ovary.

Uterus

1. The uterus is a pear-shaped organ. The uterine cavity and the cervical canal are the spaces formed by the uterus.
2. The wall of the uterus consists of the perimetrium, or serous layer; the myometrium (smooth muscle); and the endometrium.

Vagina

1. The vagina connects the uterus (cervix) to the vestibule.
2. The vagina consists of a layer of smooth muscle and an inner lining of moist stratified squamous epithelium.
3. The wall of the vagina produces lubricating fluid.
4. The hymen covers the vestibular opening of the vagina in young females.

External Genitalia

1. The vestibule is a space into which the vagina and the urethra open.
2. The clitoris is composed of erectile tissue and contains many sensory receptors important in detecting sexual stimuli.
3. The labia minora are folds that cover the vestibule and form the prepuce.

4. The greater vestibular glands produce a mucous fluid.
5. The labia majora cover the labia minora, and the pudendal cleft is a space between the labia majora.
6. The mons pubis is an elevated area superior to the labia majora.

Mammary Glands

1. Mammary glands are the organs of milk production.
2. The mammary glands are modified sweat glands that consist of glandular lobes and adipose tissue.
3. The lobes connect to the nipple through ducts. The nipple is surrounded by the areola.
4. The female breast enlarges during puberty under the influence of estrogen and progesterone.

19.6 Physiology of Female Reproduction

Puberty in Females

1. Puberty begins with the first menstrual bleeding (menarche).
2. Puberty begins when GnRH, LH, and FSH levels increase.

Menstrual Cycle

1. The cyclical changes in the uterus are controlled by estrogen and progesterone produced by the ovary.
2. Menses (from day 1 to day 4 or 5): Menstrual fluid is produced by degeneration of the endometrium.
3. Proliferative phase (from day 5 to day of ovulation): Epithelial cells multiply and form glands.
4. Secretory phase (from day of ovulation to day 28): The endometrium becomes thicker, and endometrial glands secrete. The uterus is prepared for implantation of the developing blastocyst by day 21.
5. Estrogen stimulates proliferation of the endometrium, and progesterone causes thickening of the endometrium. Decreased progesterone causes menses.
6. FSH initiates the development of the follicles.
7. Estrogen produced by the follicles stimulates GnRH, FSH, and LH secretion, and FSH and LH stimulate more estrogen secretion. This positive-feedback

mechanism causes FSH and LH levels to increase near the time of ovulation.

8. LH stimulates ovulation and formation of the corpus luteum.
9. Estrogen and progesterone inhibit LH and FSH secretion following ovulation.
10. If fertilization does not occur, progesterone secretion by the corpus luteum decreases and menses begins.
11. If fertilization does occur, the corpus luteum continues to secrete progesterone and menses does not occur.

Menopause

The cessation of the menstrual cycle is called menopause.

Female Sexual Behavior and the Female Sex Act

1. Female sex drive is partially influenced by testosterone-like hormones produced by the adrenal cortex and estrogen produced by the ovary.
2. Autonomic nerves cause erectile tissue to become engorged with blood, the vestibular glands to secrete mucus, and the vagina to produce a lubricating fluid.

Control of Pregnancy

1. Behavioral methods are effective only when used consistently.
2. Barrier methods prevent contact between sperm cell and oocyte.
3. Chemical methods prevent oocyte ovulation.
4. Surgical methods are typically permanent.

Infertility in Females

Causes of infertility in females include malfunctions of the uterine tubes, reduced hormone secretion from the pituitary or ovary, and interruption of implantation.

REMEMB ERING AND

UNDERST ANDING

1. List the functions of the male and female reproductive systems.
2. What is the scrotum? Explain the function of the dartos and cremaster muscles.
3. Where, specifically, are sperm cells produced in the testes? Describe the process of spermatogenesis.
4. Name the ducts the sperm cells traverse from their site of production to the outside of the body.
5. In which duct do sperm cells develop their ability to fertilize?
6. Name the erectile tissues of the penis, and describe how erectile tissue becomes erect.
7. State where the seminal vesicles, prostate gland, and bulbourethral glands empty into the male reproductive duct system.
8. Define emission and ejaculation.
9. Define semen. What structures give rise to secretions that make up the semen? Describe the composition of the secretions of each gland.
10. Describe where GnRH, FSH, LH, and testosterone are produced, and explain how their secretion is regulated.
11. Describe the effects of testosterone on males during puberty and in adulthood.
12. Describe the regulation of the male sex act.
13. Describe the process of follicle development and ovulation.
14. What is the corpus luteum? What happens to the corpus luteum if fertilization occurs? If fertilization does not occur?
15. Describe the normal pathway the oocyte follows after ovulation. Where does fertilization usually take place?
16. Describe the relationship among the uterus, vagina, vestibule, and external genitalia.
17. Describe the labia minora, the prepuce, the labia majora, the pudendal cleft, and the mons pubis.
18. What are the effects of estrogen and progesterone on the uterus?
19. Describe the hormonal changes that result in ovulation. Explain the sequence of events during each phase of the menstrual cycle.

20. Define menopause and female climacteric. What causes these changes?
21. List the major age-related diseases and conditions that occur in the male reproductive system.
22. List the major age-related changes that occur in the female reproductive system.
23. List the major age-related types of cancer that occur in the female reproductive system.

CRITICAL THINKING

1. If an adult male were castrated by having his testes removed, what would happen to the levels of GnRH, FSH, LH, and testosterone in his blood?
2. Birth control pills for females contain estrogen and progesterone compounds. Explain how these hormones can prevent pregnancy.
3. What changes in hormone secretion, follicle development, and uterine development would you normally expect during the secretory phase of the menstrual cycle?
4. Describe the hormonal changes you would normally expect during approximately days 12–14 of the menstrual cycle.
5. Describe the hormonal changes you would normally expect on day 15 of the menstrual cycle.
6. What will be the consequences if a drug that blocks the effect of progesterone is taken by a female 2 or 3 days following ovulation or by a female who is pregnant?
7. During menopause, which reproductive hormones are reduced in the blood and which are increased?

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

CHAPTER
20

Development, Heredity, and Aging

Prenatal development begins at fertilization. The zygote undergoes a series of cell divisions that results in the development of a embryo, which grows and develops into a fetus. Growth and development continues after birth through the various life stages of the postnatal period.

LEARN TO APPLY IT

After reading about the benefits of breast milk, Ming was determined to breastfeed her baby until he was a year old. Unfortunately, 2 weeks after her son's birth, Ming developed a serious urinary tract infection. Her physician prescribed some medication and explained that she must not breastfeed her son while taking it.

Apply

After reading about lactation in this chapter, predict the consequences if Ming stops breastfeeding for an extended time, and propose a strategy that would allow her to cease breastfeeding for a while but resume after she has finished the antibiotic.

Answers to this question and the chapter's odd-numbered Apply It questions can be found in Appendix E.

20.1 PRENATAL DEVELOPMENT

Learning Outcomes *After reading this section, you should be able to*

A. List the prenatal periods, and state the major developmental events associated with each.
B. List the postnatal periods and state the age range for each.
C. Describe the process of fertilization.
D. Describe the blastocyst.
E. Describe the process of implantation.
F. Describe placental formation.
G. Describe the maternal hormonal changes that occur during pregnancy.
H. List the three germ layers and describe their formation.
I. List the adult derivatives of each of the three germ layers.
J. Describe the formation of the neural tube and the neural crest cells.
K. Describe the formation of the limbs.
L. Describe the formation of the face.
M. Describe the formation of the digestive tract.
N. Explain how the single heart tube is divided into four chambers.

We pass through many different stages during our lifetime. These stages may be characterized by many factors, such as biological factors or social factors. When discussing the human life span from a biological perspective, we subdivide it in multiple ways. From the broadest perspective, we divide the human life span into two major periods: (1) the prenatal period and (2) the postnatal period. Each of these periods is then subdivided based on specific criteria (figure 20.1).

The **prenatal** (pree-NAY-tal; before birth) **period,** the period from fertilization to birth, can be divided into three parts:

1. The **germinal period** begins at fertilization and ends at 14 days (weeks 1 and 2 of development). This is the stage when the primitive germ layers form (discussed later in this section).
2. The **embryonic period** occurs during days 14–56 after fertilization (weeks 3–8 of development). This is the time when the major organs form. The developing human is called an **embryo** (EM-bree-oh).
3. The **fetal period** extends from 56 days after fertilization to birth (the last 30 weeks of development). During this stage, the organ systems grow and become more mature. The developing human is called a **fetus** (FEE-tus; offspring).

Figure 20.1 **The Human Life Span**

The human life span is divided into two major periods: the prenatal period and the postnatal period. These two periods are subdivided based on specific criteria.

Two methods are used to describe the age of an unborn child: (1) clinical age and (2) developmental age. To calculate the **clinical age** of an unborn child, the medical community uses the mother's **last menstrual** (MEN-stru-al) **period (LMP).** An embryo or a fetus is therefore considered to be a certain number of days post-LMP. Most embryologists, on the other hand, use **developmental age,** which begins with fertilization, to describe the timing of developmental events. Because fertilization is assumed to occur approximately 14 days after LMP, the developmental age is 14 days less than the clinical age. The times presented in this chapter are based on developmental age.

The prenatal period is acutely important for the remainder of a person's life. Essentially, early in this period the foundation of the human body is established and the first important steps of growth begin. Though these first 9 months of life are extremely important, the prenatal period is only a small part of the total life span.

The postnatal period begins at birth. This period is commonly divided into five stages:

1. **Neonatal period** extends from birth to 1 month after birth.

2. **Infancy** includes the time from 1 month to 1 or 2 years of age. The end of infancy is sometimes set at the time the child begins to walk.
3. **Childhood** includes the time from age 1 or 2 to puberty. During childhood, the individual develops considerably and forms many of the emotional characteristics that last throughout life.
4. **Adolescence** extends from puberty (age 11–14) to 20 years. Puberty usually occurs somewhat earlier in females (about age 11–13) than in males (about age 12–14). A period of rapid growth usually accompanies the onset of puberty.
5. **Adult** is the time from age 20 to death. Full adult stature is usually achieved by age 17 or 18 in females and by age 19 or 20 in males. Adulthood is sometimes divided into three periods: (1) young adult, age 20–40; (2) middle age, age 40–65; and (3) older adult, age 65 to death.

Fertilization

Fertilization is the union of a sperm cell and an oocyte, along with their genetic material (chromosomes), to produce a new individual. After sperm cells are ejaculated into the vagina, they are transported through the cervix and the body of the uterus to the uterine tubes, where fertilization occurs. The swimming ability of the sperm cells and the muscular contractions of the uterus and uterine tubes are responsible for the movement of sperm cells through the female reproductive tract. Both oxytocin released by the female posterior pituitary and prostaglandins within the semen stimulate contractions in the uterus and uterine tubes.

While passing through the uterus and the uterine tubes, the sperm cells undergo capacitation. **Capacitation** (kuh-PAS-i-tey-shun) makes the sperm cells capable of fertilization by releasing the concentrated enzymes contained in the acrosome, a region of the sperm cell head. The enzymes digest a pathway through the cumulus cells and the zona pellucida of the **secondary oocyte** (OH-oh-site; egg cell).

The secondary oocyte is capable of being fertilized for up to about 1 day after ovulation, and some sperm cells remain viable in the female reproductive tract for up to 6 days, although most of them degenerate before that time.

Apply It 1

During what days of the menstrual cycle is sexual intercourse most likely to result in pregnancy?

Figure 20.2 illustrates the process of fertilization.

PROCESS Figure

PROCESS Figure 20.2 APR **Fertilization**

Fertilization occurs when a sperm cell and oocyte combine.

Apply

If two sperm cells fertilized the same oocyte, how many chromosomes would the zygote have?

❶ Hundreds of sperm cells reach the secondary oocyte, but normally only one sperm cell can enter the secondary oocyte. Fertilization by multiple sperm cells is prevented by specific changes in the oocyte cell membrane.

❷ The secondary oocyte undergoes the second meiotic division only after a sperm cell enters it. After the second meiotic division, the oocyte nucleus moves to the center of the cell, where it meets the nucleus of the sperm cell. Each of these nuclei has 23 chromosomes.

❸ The fusion of the two nuclei, which completes the process of fertilization, produces a **zygote** (ZIE-goht; having a yoke) that has 46 chromosomes. The zygote develops into the embryo.

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Early Cell Division

About 18–36 hours after fertilization, the zygote divides by mitosis (see chapter 3) to form two cells (figure 20.3). Those two cells divide to form four cells, which divide to form eight, and so on. Even though the number of cells increases, the size of each cell decreases, so that the total mass of cells remains about the same size as the zygote. These cells have the ability to develop into a wide range of tissues. As a result, the total number of cells can be decreased, increased, or reorganized during this period without affecting normal development.

Figure 20.3 APR **Development of the Blastocyst and Implantation**

Successive cell divisions produce a multicellular morula by day 5, which becomes a hollow blastocyst on day 6. In the figure of the blastocyst, *green* cells are trophoblastic and *orange* cells are embryonic. (*a*) Zygote (120 μM in diameter with two polar bodies attached). (*b-e*) During the early cell divisions, the embryo divides into more and more cells, but the total size of the embryo remains relatively constant.

(a–e) Dr. Yorgus Nikas/Jason Burns/Phototake

In rare cases, following early cell divisions, the cells separate and form two individuals, called "identical twins," or **monozygotic** (mon-oh-zie-GOT-ik) **twins.** Identical twins therefore have identical genetic information in their cells. Identical twins can also occur by other mechanisms a little later in development. Occasionally a woman can ovulate two or more secondary oocytes at the same time. Fertilization of multiple oocytes by different sperm cells results in "fraternal twins," or **dizygotic (**DIE-zie-GOT-ik**) twins.** Even though who we are and what we look like are determined in large part by genes, identical twins—although they have the same genes—may not look exactly alike. In fact, identical twins often look more like mirror images of each other. Genes interact with minute environmental cues in the embryo and in the child to determine the final form of the individual.

Blastocyst

After fertilization, multiple cell divisions have produced an embryonic mass of about 12–16 cells, called a **morula** (MOR-you-lah; mulberry) (figure 20.3). Most of the cells of the morula will not form the embryo proper but will form support structures, such as the placenta.

When a cavity begins to appear within the mass of cells, the whole structure is called a **blastocyst** (BLAS-toh-sist) (figure 20.3*e*). The fluid-filled cavity is called the **blastocele** (BLAS-toe-seel). Most of the blastocele is surrounded by a single layer of cells, but at one end of the blastocyst, the cells are several layers thick. This thickened area of the blastocyst is called the **inner cell mass.** Not all cells of the blastocyst give rise to the new individual. The embryo proper, which will become the new individual, will develop from only a few cells of the inner cell mass. These cells are commonly referred to as **stem cells** because they give rise to all the cell types within the body. The remaining cells of the blastocyst are called the **trophoblast** (TROH-foh-blast), which forms the embryonic part of the placenta and the membranes (chorion and amnion) surrounding the embryo.

Implantation of the Blastocyst and Development of the Placenta

All these early events, from the first cell division to formation of the blastocele, occur as the embryonic mass moves from the site of fertilization in the uterine tube to the site of **implantation** (im-plan-TAY-shun) in the uterus. The endometrium of the uterus is prepared for implantation by 7 or 8 days after ovulation, when the secondary oocyte is released from the ovary. Fertilization will occur after ovulation, usually within the uterine tube. About 7 days after fertilization, the blastocyst attaches itself to the uterine wall and begins the process of implantation. The trophoblast cells of the blastocyst digest the uterine tissues as the blastocyst burrows into the uterine wall. Before implantation and for a short time afterward, the embryo is insensitive to environmental toxins. During the first few days of development, each cell has enough yolk to supply its own energy needs and requires few external nutrients. Furthermore, during the first couple of weeks of development, large numbers of cells can die, yet the embryo can fully recover.

As the blastocyst burrows into the uterine wall, trophoblast cells, called the **chorion** (KOH-ree-on), form the embryonic portion of the **placenta** (plah-SEN-tah), the organ of nutrient and waste product exchange between the embryo and the mother. Fingerlike projections, called **chorionic villi,** protrude into cavities formed within the maternal endometrium. Those cavities, called **lacunae** (la-KOO-nee), are filled with maternal blood (figure 20.4). In the mature placenta, the embryonic blood supply is separated from the maternal blood supply by the embryonic capillary wall, a basement membrane, and a thin layer of chorion. As a result, the embryonic blood and maternal blood do not mix. Nutrients and waste products must cross this semipermeable barrier between the two circulations.

Figure 20.4 **Interface Between Maternal and Fetal Circulation**

(*a*) Location of the placenta and umbilical cord in relation to the fetus. (*b*) As the chorion encounters maternal blood vessels, lacunae (cavities) form and become filled with maternal blood. In the mature placenta, the embryonic blood vessels and other tissue form chorionic villi, and nutrients are exchanged between embryonic and maternal blood. Note that the umbilical arteries and fetal arterioles contain deoxygenated blood and that the umbilical vein and fetal venules contain oxygenated blood. (*c*) Under normal conditions, the maternal and fetal blood are separated by the chorion and a basement membrane and do not mix.

Initially, the embryo is attached to the placenta by a connecting stalk. As the embryo matures, the connecting stalk elongates and becomes the **umbilical** (um-BIL-ih-kal; navel) **cord** (figure 20.4*b*). Within the umbilical cord, blood vessels carry blood from the embryo to the placenta and from the placenta to the embryo.

Maternal Hormonal Changes

Throughout the pregnancy, several hormones are secreted by the placenta as well as the ovary. These hormones are important for the maintenance of the pregnancy. Three hormones are of interest during pregnancy: (1) human chorionic gonadotropin, (2) estrogen, and (3) progesterone. Figure 20.5 illustrates the changes in the levels of secretion of these three hormones.

PROCESS Figure

PROCESS Figure 20.5 **Changes in Hormone Concentration During Pregnancy**

During pregnancy, hCG, progesterone, and estrogen are secreted. The placenta secretes hCG. Early in pregnancy, the ovary secretes estrogen and progesterone. During midpregnancy, there is a shift toward estrogen and progesterone secretion by the placenta.

Understand **Why is hCG secretion important during the first trimester?**

❶ The chorion secretes **human chorionic gonadotropin** (GOH-nad-oh-TROH-pin) **(hCG),** which travels in the blood to the maternal ovary and causes the corpus luteum to remain functional. The secretion of hCG begins shortly after implantation, increases rapidly, and reaches a peak about 8 or 9 weeks after fertilization. Subsequently, hCG levels decline to a lower level, where they are maintained throughout the remainder of the pregnancy. Most pregnancy tests are designed to detect hCG in either urine or blood.

❷ Progesterone secretion increases during most of the pregnancy until it levels off near the end of the pregnancy.

❸ Estrogen levels increase slowly throughout pregnancy, with a more rapid increase as the time of birth approaches.

The estrogen and progesterone are secreted by the corpus luteum of the ovary early in the pregnancy (see chapter 19) and are essential for maintaining the endometrium for the first 3 months of pregnancy. After the placenta forms, it also begins to secrete estrogen and progesterone. By the third month of pregnancy, the placenta has become an endocrine gland that secretes sufficient quantities of estrogen and progesterone to maintain pregnancy, and the corpus luteum is no longer needed.

Formation of the Germ Layers

After implantation, a new cavity, called the **amniotic** (am-nee-OT-ik) **cavity,** forms inside the inner cell mass and causes the part of the inner cell mass nearest the blastocele to separate as a flat disk of tissue called the **embryonic disk** (figure 20.6). The amniotic cavity is bounded by a membrane called the **amnion** and is filled with **amniotic fluid.** The embryo will grow in the amniotic cavity, where the amniotic fluid forms a protective cushion. The embryonic disk at first is composed of two layers of cells: (1) an **epiblast** adjacent to the amniotic cavity and (2) a **hypoblast** on the side of the disk opposite the amniotic cavity. A third cavity, the **yolk sac,** forms inside the blastocele from the hypoblast.

Figure 20.6 **Early Embryo and Surrounding Structures in the Placenta**
The embryonic disk consists of epiblast and hypoblast surrounded by the amniotic cavity and yolk sac. The connecting stalk, which attaches the embryo to the uterus, becomes part of the umbilical cord.

At about 14 days after fertilization, the embryonic disk has become a slightly elongated, oval structure. Some of the epiblast cells migrate toward the center of the disk, forming a thickened line called the **primitive streak**. The formation of the primitive streak establishes the central axis of the embryo. At this point, **gastrulation** occurs, which involves movement of cells to form three distinct germ layers. Figure 20.7 illustrates the process of gastrulation.

PROCESS Figure

PROCESS Figure 20.7 **Primitive Streak and Germ Layers**
During gastrulation, three germ layers form: the ectoderm, the mesoderm, and the endoderm.

Understand **How are the three germ layers depicted in this figure related to the two layers of the embryonic disk that are depicted in figure 20.5?**

❶ Some of the epiblast cells migrate through the primitive streak. The remaining epiblast cells form the **ectoderm** (EK-toe-derm; outside layer).

❷ Of these migrating cells, some displace the hypoblast to form the **endoderm** (EN-doh-derm; inside layer).

❸ Other migrating cells emerge between the epiblast and endoderm as a new germ layer, called the **mesoderm** (MEZ-oh-derm; middle layer).

The embryo is now three-layered, having ectoderm, mesoderm, and endoderm. All the tissues of an adult can be traced to these three germ layers (table 20.1).

Table 20.1 Tissues Derived from Each Germ Layer

Endoderm	Ectoderm	Mesoderm
Lining of digestive tract	Epidermis of skin	Dermis of skin
Lining of lungs	Tooth enamel	Heart and blood vessels
Lining of hepatic, pancreatic, and other exocrine ducts	Lens and cornea of eye	Parenchyma (substance) of glands
Kidney ducts and urinary bladder	Nasal cavity	Kidneys
Thymus	Anterior pituitary	Gonads
Thyroid gland	Neuroectoderm	Muscle
Parathyroid glands	Brain and spinal cord	Bones (except facial)
Tonsils	Somatic motor neurons	Microglia
	Preganglionic autonomic neurons	
	Posterior pituitary	
	Glial cells (except microglia)	
	Neural crest cells	
	Melanocytes	
	Sensory neurons	
	Postganglionic autonomic neurons	
	Adrenal medulla	
	Facial bones	
	Teeth (dentin, pulp, and cementum) and gingiva	
	A few skeletal muscles in head	

From about day 14 until about day 35, the embryo is at maximum risk from environmental toxins and drugs that can cause birth defects. The causes of birth defects are a major unsolved issue in biology at present. However, it appears that oxidative damage to key molecules in certain developing cells and/or changes in the DNA function within those cells may be involved.

A specialized group of cells at the cephalic (towards the head) end of the primitive streak moves from one end of the primitive streak to the other and, in some yet unknown way, organizes the embryo. A cordlike structure called the **notochord** (NOH-toh-kord) is formed by these specialized cells as they move down the primitive streak. The notochord marks the central axis of the developing embryo (figure 20.7).

Apply It 2

Describe the result if two primitive streaks form in one embryonic disk. What if the two primitive streaks are touching each other?

Neural Tube and Neural Crest Formation

The development of portions of the nervous system involves the specialization of ectoderm. The process is illustrated in figure 20.8.

PROCESS Figure

PROCESS Figure 20.8 **Formation of the Neural Tube**

The neural folds, which consist of neuroectoderm, come together at the midline and fuse to form a neural tube. This fusion begins in the center and moves both cranially and caudally. (*a*) The embryo shown is about 21 days after fertilization. (*b*) These cross sections represent progressive closure of the neural tube.

Explain the difference between the notochord and the neural tube.

❶ At about 18 days after fertilization, the ectoderm overlying the notochord thickens to form the **neural plate.**

❷ The lateral edges of the plate begin to rise like two ocean waves coming together. These edges are called the **neural folds,** and between them lies a **neural groove.**

❸ The neural folds begin to meet in the midline and fuse into a **neural tube**. The cells of the neural tube are called **neuroectoderm** (noor-oh-EK-toh-derm) (table 20.1). As the neural folds come together and fuse, a population of cells breaks away from the neuroectoderm all along the crests of the folds. Most of these **neural crest cells** become part of the peripheral nervous system or become melanocytes in the skin. In the head, neural crest cells also contribute to the skull, the dentin of teeth, blood vessels, and general connective tissue.

❹ Neuroectoderm becomes the brain, the spinal cord, and parts of the peripheral nervous system. The neural tube becomes completely closed by day 26. If the neural tube fails to close, major defects of the central nervous system can result.

CLINICAL IMPACT

In Vitro Fertilization and Embryo Transfer

In a small number of women, normal pregnancy is not possible because of an anatomical or physiological condition. In 87% of these cases, the uterine tubes are incapable of transporting the zygote to the uterus or allowing sperm

cells to reach the oocyte. Since 1978, in vitro fertilization and embryo transfer have made pregnancy possible in hundreds of such women. **In vitro fertilization (IVF)** involves removing secondary oocytes from a woman, placing the oocytes into a petri dish, and adding sperm cells to the dish, where fertilization and early development occur in vitro, which means "in glass." **Embryo transfer** involves removing the developing embryo from the petri dish and introducing the embryo into the uterus of a recipient woman.

For in vitro fertilization and embryo transfer to be accomplished, a woman is first injected with a substance similar to luteinizing hormone (LH), which causes more than one follicle to ovulate at a time. Just before the follicles rupture, the secondary oocytes are surgically removed from the ovary. The oocytes are then incubated in a dish and maintained at body temperature for 6 hours. Then, sperm cells are added to the dish. Different techniques may then be utilized that enhance sperm entry into the oocyte.

After 24–48 hours, several of the embryos are transferred to the uterus. Multiple embryos are introduced into the uterus to increase the success rate as much as possible, because only a few of them survive. The woman is usually required to lie perfectly still for several hours after the embryos have been introduced into the uterus to prevent possible expulsion before implantation can occur. It is not fully understood why such expulsion does not occur in natural fertilization and implantation. Implantation and subsequent development then proceed in the uterus as they would for natural implantation.

The success rate of embryo transfer varies from clinic to clinic, with the age of the embryo at the time of transfer, and with the age of the patient. The current success rate for achieving pregnancy following IVF is 31%. Of these pregnancies, 83% result in live births. Multiple births have occurred frequently following embryo transfer because of the practice of introducing more than one embryo into the uterus.

Anencephaly (AN-en-SEF-ah-lee; no brain) is a birth defect wherein much of the brain fails to form because the neural tube did not close in the region of the head. A baby born with anencephaly cannot survive. **Spina bifida** (SPY-nah BIH-fih-dah; split spine) is a general term describing defects of the spinal cord or vertebral column. Spina bifida can range from a simple defect with one or more vertebral spinous processes split or missing but no clinical manifestation to a more severe defect that can result in paralysis of the limbs or the bowels and bladder, depending on where the defect occurs. More severe forms of spina bifida result from failure of the neural tube in the area of the spinal cord to close. It has been demonstrated that adequate amounts of the B vitamin folate, more commonly referred to as folic acid, in the diet during pregnancy can reduce the risk of such defects.

Formation of the General Body Structure

Arms and legs first appear at about 28 days after fertilization as **limb buds** (figure 20.9) and quickly begin to elongate. At about 35 days, expansions called hand and foot plates form at the ends of the limb buds. Zones of cell death between the future fingers and toes of the hand and foot plates help sculpt the fingers and toes.

Figure 20.9 **Human Embryo 35 Days After Fertilization**
Limb buds begin to form about 28 days after fertilization.
John Giannicchi/Science Source

The face develops by fusion of five growing masses of tissue, called **processes** (figure 20.10). A single **frontonasal process** forms the forehead, nose, and center of the upper jaw and lip. Two **maxillary processes** form the maxillae (upper lip and jaw), and two **mandibular processes** form the mandible (lower lip and jaw).

The nose begins as two structures, one on each side of the forehead mass. As the brain enlarges and the face matures, the two parts of the nose approach each other in the midline and fuse (figure 20.10*b*). The two masses forming the upper jaw expand toward the midline and fuse with part of the nose to form the upper jaw and lip (figure 20.10*c*). A **cleft lip** results from failure of these structures to fuse. Cleft lips usually do not occur in the midline, but to one side (or both sides). The cleft can vary in severity from a slight indentation in the lip to a fissure that extends from the mouth to the nares (nostril).

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Figure 20.10 **Development of the Face**

(*a*) The face develops from five processes that enlarge and fuse together. These processes are the single frontonasal process (indicated in *upper* blue *area*), the two maxillary processes (indicated in *middle* yellow *area*) and the two mandibular processes (indicated in *lower red area*). (*b*) 33 days after fertilization, two areas that will form the nose are visible. (*c*) At 14 weeks after fertilization, the processes have fused to form structures of the face.

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The roof of the mouth, or palate, begins to form as vertical shelves of tissue that grow on the inside of the maxillary masses. These shelves swing to a horizontal position and begin to fuse with each other at about 56 days of development. If the palate does not fuse, a midline cleft in the roof of the mouth called a **cleft palate** results. A cleft palate can range in severity from a slight cleft of the uvula to a fissure extending the entire length of the palate. A cleft lip and cleft palate can occur together, forming a continuous fissure.

Development of the Organ Systems

The major organ systems appear and begin to develop during the embryonic period (second to eighth week of development). This period is therefore also called the period of **organogenesis** (OR-gah-noh-JEN-eh-sis). The individual organ systems are listed in table 20.2; only general comments about a few select systems are presented in the text.

TABLE 20.2 Development of the Organ Systems

Age (Days Since Fertilization)							
	1–5	**6–10**	**11–15**	**16–20**	**21–25**	**26–30**	**31-**
General Features	Fertilization, blastocyst	Blastocyst implants.	Primitive streak, three germ layers	Neural plate	Neural tube closed	Limb buds and other "buds" appear.	Har

Age (Days Since Fertilization)							
	1–5	6–10	11–15	16–20	21–25	26–30	31-
Integumentary System			Ectoderm, mesoderm		Melanocytes form from neural crest.		Sen
Skeletal System			Mesoderm		Neural crest cells (form facial bones)	Limb buds	Mes
Muscular System			Mesoderm	Somites (body segments) begin to form.		Somites are all formed.	Mus
Nervous System			Ectoderm	Neural plate	Neural tube complete; neural crest forms; eyes and ears begin to form.	Lens begins to form.	Ner
Endocrine System			Ectoderm, mesoderm, endoderm	Thyroid begins to develop.		Parathyroid glands and pancreas appear.	Pitu
Cardiovascular System			Mesoderm	Blood islands form; two-tubed heart forms.	Single-tubed heart begins to beat.	Interatrial septum forms.	Inte
Lymphatic System			Mesoderm			Thymus appears.	Lar
Respiratory System			Mesoderm, endoderm		Diaphragm begins to form.	Trachea, lung buds appear.	Sec
Digestive System			Mesoderm, endoderm		Tooth dentin forms; foregut and hindgut form.	Liver and pancreas appear as buds; tongue bud appears.	Mou
Urinary System			Mesoderm, endoderm		Embryonic kidneys appear.	Embryonic kidneys elongate.	Adu
Reproductive System			Mesoderm, endoderm		Primordial germ cells form on yolk sac.	Male reproductive ducts appear; external genital structures begin to form.	

While the neural tube is forming (18–26 days), the remainder of the embryo is folding to form a tube along the upper part of the yolk sac (figure 20.11). The developing digestive tract pinches off from the yolk sac as a tube but remains attached in the center to the yolk sac by a structure called a yolk stalk.

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Figure 20.11 **Development of the Digestive Tract**

The digestive tract develops along the dorsal side of the yolk sac (*yellow*) as the body folds into a tube (*blue arrows*). The figures in back are shown in sagittal section. The figures in front are shown in cross section. The *dashed line* on the figures in back shows the plane of section in the figures in front. (*a*) An early embryo (about 24 days). (*b*) A slightly older embryo (about 28 days).

A considerable number of outpocketings appear at about 28 days after fertilization along the entire length of the digestive tract (figure 20.12). A surprisingly large number of important internal organs develop from those outpocketings, including the auditory tubes, tonsils, thymus, anterior pituitary gland, thyroid gland, parathyroid glands, lungs, liver, pancreas, and urinary bladder.

Figure 20.12 **Embryonic Digestive and Urinary Systems**

Outpocketings of the digestive tract (*tan*) form many adult structures, such as the lungs and glands. The embryonic kidney is also shown (*purple*).

The heart develops from two blood vessels, which lie side by side in the early embryo.Figure 20.13 illustrates the development of the heart.

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PROCESS Figure

PROCESS Figure 20.13 **Formation of the Heart**

The four-chambered adult heart develops from two parallel vessels that merge.

Why are interatrial septal defects more common than interventricular septal defects?

❶ At about 21 days after fertilization the two blood vessels fuse. The fused blood vessels expand and bend within the confined space of the pericardium to form a single, midline heart. At about this time, the primitive heart begins to beat. Blood vessels form from "blood islands" on the surface of the yolk sac and inside the embryo. These islands expand and fuse to form the circulatory system.

❷ The major chambers of the heart, the atrium and ventricle, expand rapidly. At first, there is a single atrium and single ventricle. At about 31 days after fertilization, partitions begin to grow toward the center of the heart.

❸ The single ventricle is subdivided into two chambers by the development of an **interventricular** (IN-ter-ven-TRIK-you-lar) **septum**. If the interventricular septum does not grow enough to completely separate the ventricles, a ventricular septal defect results. An **interatrial** (IN-ter-AY-tree-al) **septum** forms to separate the two atria.

❹ An opening in the interatrial septum called the **foramen ovale** (oh-VAL-ee) connects the two atria and allows blood to flow from the right to the left atrium in the fetus.

❺ Because of the foramen ovale, some blood in the fetus passes from the right atrium to the left atrium and bypasses the right ventricle and the lungs.

The foramen ovale normally closes off at the time of birth, and blood then circulates through the right ventricle and the lungs. If this does not occur, an interatrial septal defect occurs. An interatrial septal defect or an interventricular septal defect usually results in a heart murmur.

The kidneys develop from mesoderm located along the lateral wall of the body cavity (see figure 20.12). The embryonic kidneys are much more extensive than the adult kidneys, extending the entire length of the body cavity. They are closely associated with internal reproductive organs, such as the ovaries or testes, and reproductive ducts, such as the uterine tubes or ductus deferens. Most of the embryonic kidneys degenerate, with only a very small part forming the adult kidney.

Growth of the Fetus

The embryo becomes a fetus about 8 weeks after fertilization (figure 20.14). The beginning of the fetal period is marked by the beginning of bone ossification. In the embryo, most of the organ systems are developing, whereas in the fetus the organs are present. During the fetal period, the organ systems enlarge and mature. The fetus grows from about 3 cm and 2.5 g (0.09 oz) at 8 weeks to 50 cm and 3300 g (7 lb, 4 oz) at the end of pregnancy. The growth during the fetal period represents more than a 15-fold increase in length and a 1400-fold increase in weight.

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Figure 20.14 **Late Embryo and Fetus**
(*a*) Embryo at 50 days of development. (*b*) Fetus at 3 months of development. (*c*) Fetus at 4 months after fertilization.
(a) Claude Edelmann/Science Source; (b) Petit Format/Nestle/Science Source; (c) Tissuepix/Science Source

The amniotic fluid contains toxic waste products from the fetus's digestive tract and kidneys. Fine, soft hair called **lanugo** (la-NOO-goh) covers the fetus, and a waxy coat of loose epithelial cells called

vernix caseosa (VER-niks kay-see-OH-sah) forms a protective layer between the fetus and the amniotic fluid.

Subcutaneous adipose tissue that accumulates in the fetus provides a nutrient reserve, helps insulate, and aids the newborn in sucking by strengthening and supporting the cheeks, so that a small vacuum can be developed in the oral cavity.

Peak body growth occurs late in gestation, but as the placenta reaches its maximum size, the O_2 and nutrient supply to the fetus becomes limited. Growth of the placenta essentially stops at about 35 weeks, limiting fetal growth.

At approximately 38 weeks of development, the fetus is ready to be delivered. The average weight at this point is 3250 g (7 lb, 2 oz) for a female fetus and 3300 g (7 lb, 4 oz) for a male fetus.

20.2 Parturition

Learning Outcome *After reading this section, you should be able to*

A. Explain the events that occur during parturition.

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Physicians usually calculate the **gestation** (jes-TAY-shun) **period** (length of pregnancy) as 280 days (40 weeks, or 10 lunar months) from the LMP to the date of delivery of the fetus. **Parturition** (par-toor-ISH-un) is the process by which the baby is born (figure 20.15). Near the end of pregnancy, the uterus becomes progressively more excitable and usually exhibits occasional contractions that become stronger and more frequent until parturition is initiated. The cervix gradually dilates, and strong uterine contractions help expel the fetus from the uterus through the vagina.

PROCESS Figure

PROCESS Figure 20.15 APR **Parturition**

During parturition, the fetus as well as the placenta are expelled from the uterus.

Understand **What hormone is given to women to increase the rate of uterine contractions during labor?**

Labor is the period during which uterine contractions occur that result in expulsion of the fetus. Although labor may differ greatly from woman to woman and from one pregnancy to another for the same woman, it can usually be divided into three stages.

Figure 20.15 illustrates the three stages of labor.

1. The **first stage** of labor, often called the *dilation phase,* begins with the onset of regular uterine contractions and extends until the cervix dilates to a diameter about the size of the fetus's head (10 cm). This stage takes approximately 24 hours, but it may be as short as a few minutes in some

women who have had more than one child. During this phase, the amnion surrounding the fetus ruptures, and amniotic fluid flows through the vagina to the exterior. This event is commonly referred to as the "water breaking" and usually occurs naturally, but the amnion may need to be ruptured artificially.

❷ The **second stage** of labor, often called the *expulsion phase,* lasts from the time of maximum cervical dilation until the time the baby exits the vagina. This stage may last from 1 minute to 1 hour or more. During this stage, contraction of the woman's abdominal muscles assists the uterine contractions.

❸ The **third stage** of labor, often called the *placental stage,* involves the expulsion of the placenta from the uterus. Contractions of the uterus cause the placenta to tear away from the wall of the uterus. Some bleeding from the uterine wall occurs because of the intimate contact between the placenta and the uterus. However, bleeding is normally limited because uterine smooth muscle contractions compress the blood vessels.

Understand ***Apply It 3***

Compare and contrast clinical age and developmental age for fertilization, implantation, the beginning of the fetal period, and parturition.

During the 4 or 5 weeks following parturition, the uterus becomes much smaller, but it remains somewhat larger than it was before pregnancy. A vaginal discharge composed of blood and degenerating endometrium can persist for several weeks after parturition.

The precise signal that triggers parturition is unknown, but many factors that support it have been identified. Figure 20.16 illustrates the interactions of chemical signals from both the mother and fetus that are involved in stimulating parturition.

PROCESS Figure

PROCESS Figure 20.16 **Factors That Influence Parturition**

Although the precise control of parturition in humans is unknown, these changes appear to play a role.

Understand **Progesterone, estrogen, prostaglandins, and oxytocin all have important roles that influence parturition. For each of these substances, describe whether it has a stimulatory or an inhibitory effect on the uterus.**

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❶ Before parturition, the progesterone concentration in the mother's blood has reached its highest level. Progesterone has an inhibitory effect on uterine smooth muscle cells. However, estrogen levels continually increase in the maternal blood, stimulating uterine smooth muscle. Thus, the inhibitory influence of progesterone on smooth muscle is overcome by the stimulatory effect of estrogen near the end of pregnancy.

❷ The fetus also plays a role in stimulating parturition. Stress on the fetus triggers the secretion of a releasing hormone from the fetal hypothalamus, which in turn causes adrenocorticotropic hormone (ACTH) to be released from the fetal anterior pituitary.

❸ ACTH stimulates the fetal adrenal gland to secrete hormones from the adrenal cortex that affect hormonal secretion by the placenta.

❹ Specifically, hormones secreted by the fetal adrenal gland reduce progesterone secretion, increase estrogen secretion, and increase prostaglandin production by the placenta. Prostaglandins strongly stimulate uterine contractions.

❺ During parturition, stretching of the uterine cervix initiates nervous reflexes that cause the mother's posterior pituitary gland to release oxytocin.

❻ Oxytocin stimulates uterine contractions, which move the fetus farther into the cervix, causing further stretch. A positive-feedback mechanism is established. This positive-feedback mechanism stops after delivery, when the cervix is no longer stretched.

20.3 THE NEWBORN

Learning Outcome *After reading this section, you should be able to*

A. Discuss the respiratory, circulatory, and digestive changes that occur in the newborn at the time of birth.

The newborn, or **neonate** (NEE-oh-nate; newborn), experiences several dramatic changes at the time of birth. The major and earliest changes are the separation of the infant from the maternal circulation and the transfer from a fluid to a gaseous environment.

Respiratory and Circulatory Changes

The large, forced gasps of air that occur when an infant cries at the time of delivery help inflate the lungs. The fetal lungs produce a substance called **surfactant** (ser-FAK-tant), which coats the inner surface of the alveoli, reduces surface tension in the lungs, and allows the newborn lungs to inflate (see chapter 15).

Surfactant is not manufactured in the fetal lungs before about 6 months after fertilization. If a fetus is born before the lungs can produce surfactant, the surface tension inside the lungs is too great for the lungs to inflate. Under these conditions, the newborn may die of respiratory distress. Therefore, premature newborns are treated with bovine or synthetic surfactant.

The initial inflation of the lungs causes important changes in the cardiovascular system. Figure 20.17*a* illustrates circulatory conditions in the fetus that will change at birth.

❶ In the fetal circulation, blood bypasses the lungs by flowing from the pulmonary trunk through the **ductus arteriosus** (DUK-tus ar-TEER-ee-oh-sus), a short artery that carries blood directly to the aorta.

❷ Blood also bypasses the lungs by flowing from the right atrium directly to the left atrium through the foramen ovale.

❸ Blood bypasses the liver sinusoids by flowing through the **ductus venosus** (vee-NOH-sus), which connects to the inferior vena cava.

❹ Oxygenated blood from the placenta is passed to the fetus by the **umbilical vein**.

❺ Deoxygenated blood is carried from the fetus to the placenta through the **umbilical arteries**.

Figure 20.17*b* illustrates circulatory changes that occur at birth.

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PROCESS Figure

PROCESS Figure 20.17 **Circulation in the Fetus and Newborn**

(*a*) Circulatory conditions in the fetus.

(*b*) Circulatory changes that occur after birth.

Understand **Describe the blood oxygen characteristics of the umbilical arteries and veins. How is this different from the normal blood oxygen levels in the arteries and veins after birth?**

❶ When air enters the lungs, blood is forced through the pulmonary arteries to the lungs. The ductus arteriosus closes and is replaced with connective tissue.

❷ Changes in blood flow resistance in the lungs and blood volume and blood pressure in the heart chambers allow for the closing of the foramen ovale of the fetal heart, separating the heart into two pumps. Expansion of the lungs reduces the resistance to blood flow through the lungs. As a result, there is increased blood flow from the right ventricle of the heart through the pulmonary arteries. Consequently, an increased amount of blood flows from the right atrium to the right ventricle and into the pulmonary arteries, and less blood flows from the right atrium through the foramen ovale to the left atrium. There is also an increase in the volume of blood returning from the lungs

through the pulmonary veins to the left atrium. This increased volume makes the pressure in the left atrium greater than that in the right atrium. This pressure difference forces blood against the interatrial septum, closing a flap of tissue that develops in that region over the foramen ovale. This action completes the separation of the heart into two pumps: the right side and the left side of the heart.

❸ When the umbilical cord is tied and cut, no more blood flows through the ductus venosus, umbilical vein, or umbilical arteries. The ductus venosus degenerates and becomes the ligamentum venosum.

❹ The umbilical veins become the round ligament of the liver.

❺ The umbilical arteries degenerate.

Digestive Changes

Late in gestation, the fetus swallows amniotic fluid from time to time. Shortly after birth, this swallowed fluid plus cells sloughed from the mucosal lining of the digestive tract, mucus produced by intestinal mucous glands, and bile from the liver are eliminated as a greenish anal discharge called **meconium** (meh-KOH-nee-um).

After birth, the neonate is suddenly separated from its source of nutrients, the maternal circulation. Because of this separation and the shock of birth, the neonate usually loses 5–10% of its total body weight during the first few days of life. Although the digestive system of the fetus becomes somewhat functional late in development, it is still very immature in comparison to that of the adult and can digest only a limited number of food types. The newborn digestive system is capable of digesting lactose (milk sugar) from the time of birth. The pancreatic secretions are sufficiently mature for a milk diet, but the digestive system only gradually develops the ability to digest more solid foods over the first year or two. New foods should therefore be introduced gradually during the first 2 years. Parents are also advised to introduce only one new food at a time, so that, if an allergic reaction occurs, the cause is more easily determined.

Amylase secretion by the salivary glands and the pancreas remains low until after the first year. Lactase activity in the small intestine is high at birth but declines during infancy, although the levels still exceed those in adults. In many adults, lactase activity is lost, and an intolerance to milk develops.

20.4 LACTATION

Learning Outcome *After reading this section, you should be able to*

A. Describe the events of lactation.

Lactation (lak-TAY-shun) is the production of milk by the mammary glands. It normally occurs in women following parturition and may continue for up to 2 or 3 years.

During pregnancy, the high concentration and continuous presence of estrogen and progesterone cause expansion of the duct system and the secretory units within the breast. Other hormones, including a prolactin-like hormone produced by the placenta, help support the development of the breasts. Also, additional adipose tissue is deposited; thus, the size of the breasts increases throughout pregnancy. Estrogen and progesterone prevent the secretory part of the breast from producing milk during pregnancy.

Blood levels of estrogen and progesterone fall dramatically after parturition. Once the placenta has been dislodged from the uterus, the source of these hormones is gone. After parturition, in the absence of estrogen and progesterone, prolactin produced by the anterior pituitary stimulates milk production.

Figure 20.18 illustrates the hormonal control of lactation.

PROCESS Figure

PROCESS Figure 20.18 APR **Hormonal Control of Lactation**

Hormones regulate the production and release of milk from the mammary glands.

Understand **Identify the target tissues for prolactin and oxytocin. Why are both hormones necessary for normal lactation?**

❶ During suckling, sensory action potentials are sent from the nipple to the hypothalamus.

❷ In response, the hypothalamus stimulates the release of prolactin from the anterior pituitary and oxytocin from the posterior pituitary.

❸ Prolactin stimulates milk production in alveoli of the mammary glands. Oxytocin stimulates smooth muscle cells associated with the alveoli and ducts of the mammary glands to contract. As a result, milk flows from the breast, in a process called **milk letdown**.

For the first few days following parturition, the mammary glands secrete **colostrum** (koh-LOSS-trum), a high-protein material that contains many antibodies. Although colostrum is high in proteins, it contains little fat and less lactose than milk. Eventually, milk with a higher fat and lactose content is produced. Colostrum and milk provide nutrition and antibodies that help protect the baby from infections.

At the time of breastfeeding, milk contained in the alveoli and ducts of the breast is forced out of the breast by contractions of cells surrounding the alveoli. As described earlier, suckling causes the release of oxytocin from the posterior pituitary. Higher brain centers can also cause the release of oxytocin as a result of a conditioned reflex in response to such stimuli as hearing an infant cry or thinking about breastfeeding.

Repeated stimulation of prolactin release makes breastfeeding possible for several years. If breastfeeding is stopped, prolactin release stops, and within a few days the breasts' ability to respond to prolactin is lost, and milk production ceases. This information may be helpful in answering the Learn to Apply it at the beginning of the chapter.

Apply ***Apply It 4***

While breastfeeding her baby, a woman felt cramps in her abdomen. Explain what was happening.

20.5 FIRST YEAR FOLLOWING BIRTH

Learning Outcome *After reading this section, you should be able to*

A. Describe the changes that occur during the first year after birth.

A great number of changes occur in the infant from the time of birth until 1 year of age. The time when these changes occur may vary considerably from child to child, and the dates given are only rough estimates. The brain is still developing at this time, and much of what the infant can accomplish depends on the amount of brain development achieved. It is estimated that the newborn's central nervous system contains nearly all the adult number of neurons, but subsequent growth and maturation of the brain add new glial cells, new myelin sheaths, and new connections between neurons, which may continue throughout life.

By 6 weeks, the baby is usually able to hold up her head when placed in a prone position and begins to smile in response to people or objects. At 3 months of age, the infant exercises his limbs aimlessly. However, he can control his arms and hands enough that voluntary thumb sucking can occur. The infant can follow a moving person with his eyes. At 4 months, the infant begins to do push-ups—that is, raise himself by the arms. The infant can begin to grasp objects placed in his hands, coo and gurgle, roll from back to side, listen quietly when hearing a person's voice or music, hold the head erect, and play with his hands. At 5 months, the infant can usually laugh out loud, reach for objects, turn her head to follow an object, lift her head and shoulders, sit with support, and roll over. At 8 months, the infant can recognize familiar people, sit up without support, and reach for specific objects. At 12 months, the infant may pull herself to a standing position and may be able to walk without support. The child can pick up objects in her hands and examine them carefully. A 12-month-old child can understand much of what is said and may say several words.

20.6 LIFE STAGES

Learning Outcomes *After reading this section, you should be able to*

A. Describe the major events associated with each of the following stages: child, adolescent, adult.
B. Describe the process of aging.
C. Describe the events that occur at the time of death.

After the first year of life, an individual will pass through several life stages: child, adolescent, and adult. During childhood, the individual grows in size and develops considerably. Many of the emotional characteristics a person possesses throughout life are formed during early childhood.

Major physical and physiological changes occur during adolescence, and many of these changes also affect the emotions and behavior of the individual. Other emotional changes occur as the adolescent attempts to fit into an adult world. **Puberty** (PYU-ber-tee) is the time when reproductive cells begin to mature and when gonadal hormones are first secreted in substantial amounts. These hormones stimulate the development and maturation of secondary sexual characteristics, such as enlargement of the female breasts and growth of body hair in both sexes. Puberty usually begins in females at about 11–13 years of age and in males at about 12–14 years of age. The onset of puberty is usually accompanied by a growth spurt, followed by a period of slower growth. Full adult stature is usually achieved before age 17 or 18 in females and before age 19 or 20 in males.

The Aging Process

Development of a new human begins at fertilization, and so does the process of aging. Cell division occurs at an extremely rapid rate during early development and then begins to slow as various cells become committed to specific functions within the body.

Many cells of the body, such as skin cells, continue to divide throughout life, replacing dead or damaged tissue. But other cells, such as mature neurons in the brain, cease to divide. Dead neurons tend not to be replaced. After the number of neurons reaches a peak (at approximately the time of

birth), the number begins to decline. Neuronal loss is most rapid early in life and then decreases to a slower, steady rate.

Young embryonic tissue has relatively small amounts of collagen, and the collagen that is present is not highly cross-linked, making it very flexible and elastic. However, many of the collagen fibers produced during development are permanent components of the individual. As the individual ages, more and more cross-links form between the collagen molecules, rendering the tissues more rigid and less flexible.

The tissues with the highest collagen content and the greatest dependency on collagen for their function are the most severely affected by the collagen cross-linking and tissue rigidity associated with aging. One of the first structures to exhibit age-related changes as a result of this increased rigidity is the lens of the eye. Seeing close objects becomes more difficult with advancing age until most middle-aged people require reading glasses (see chapter 9). Loss of elasticity also affects other tissues, including the joints, kidneys, lungs, and heart, and greatly reduces their functional ability.

As with nervous tissue, the number of skeletal muscle fibers declines with age. The strength of skeletal muscle reaches a peak between 20 and 35 years of life and usually declines steadily thereafter. Skeletal muscle strength depends primarily on the size of the muscle fibers, but the total number of fibers is probably also important to muscle strength. As most people age, both the number of fibers and the size of each tend to decline. The decline in muscle fiber size may be more related to a general decrease in activity than to any specific age-related changes. Like the collagen of connective tissue, however, the macromolecules of skeletal muscle cells undergo biochemical changes during aging, rendering the muscle tissue less functional. A good exercise program can slow or even partially reverse the process of muscular aging.

Cardiac muscle cells also do not normally divide after birth. Age-related changes in cardiac muscle cell function probably contribute to a decline in cardiac function with advancing age. The heart loses elastic recoil ability and muscular contractility. As a result, total cardiac output declines, and less O_2 and fewer nutrients reach the body cells supplied by the cardiovascular system. This decline in blood flow can be particularly harmful to cells that require high O_2 levels, such as neurons of the brain, and cells that are already compromised, such as cartilage cells of the joints, contributing to the general decline in these tissues.

Reduced cardiac function also can result in decreased blood flow to the kidneys, contributing to decreases in the kidneys' filtration ability. Degeneration of the connective tissues as a result of collagen cross-linking and other factors also decreases the filtration efficiency of the glomerular basement membrane.

Arteriosclerosis (ar-TEER-ee-oh-skler-OH-sis) is general hardening of the arteries affecting mainly arterioles. **Atherosclerosis** (ATH-er-oh-skler-OH-sis) is the gradual formation of lipid-containing plaques in the arterial wall of large and medium-sized arteries (see chapter 13). These plaques then may become fibrotic and calcified, resulting in arteriosclerosis. Atherosclerosis interferes with normal blood flow and may result in a **thrombosis** (throm-BOH-sis), the formation of a clot or plaque inside a vessel. An **embolus** (EM-boh-lus; a patch) is a piece of a clot that has broken loose and floats through the circulation. An embolus can lodge in smaller arteries and cause heart attacks or strokes. Although atherosclerosis affects all middle-aged and elderly people to some extent and can even occur in young people, some people appear more at risk because of high blood cholesterol levels. This condition seems to have a hereditary component, and blood tests are available to screen people for high blood cholesterol levels.

Many other organs, including the liver, pancreas, stomach, and colon, undergo degenerative changes with age. The ingestion of harmful agents can accelerate such changes. Examples of these types of accelerated changes are the degenerative changes induced in the lungs (aside from lung cancer) by cigarette smoke and sclerotic changes in the liver resulting from excessive alcohol consumption.

In addition to the previously described changes, cellular wear and tear, or cellular aging, contributes to aging. Progressive damage from many sources, such as radiation and toxic substances, can result in irreversible cellular insults and may be one of the major factors leading to aging. Although the data are

mixed and their interpretation is controversial, some studies suggest that ingesting moderate amounts of vitamins E and C in combination may help slow aging by stimulating cell repair. Vitamin C also stimulates collagen production and may slow the loss of tissue elasticity associated with aging collagen.

According to the **free radical theory of aging,** free radicals, which are atoms or molecules with an unpaired electron, can react with and alter the structure of molecules that are critical for normal cell function. Alteration of these molecules can result in cell dysfunction, cancer, or other types of cellular damage. Free radicals are produced as a normal part of metabolism and are introduced into the body from the environment through the air we breathe and the food we eat. The damage caused by free radicals may accumulate with age. Antioxidants, such as beta carotene (provitamin A), vitamin C, and vitamin E, can donate electrons to free radicals without themselves becoming harmful. Thus, antioxidants may prevent the damage caused by the free radicals and may ward off age-related disorders ranging from wrinkles to cancer. Again, the data are mixed and their interpretation is controversial.

One characteristic of aging is an overall decrease in ATP production. This decline is associated with a decrease in oxidative phosphorylation, which has been shown in many cases to be associated with **mitochondrial DNA mutations.**

Immune system changes may also be a major contributing factor to aging. The aging immune system loses its ability to respond to outside antigens and begins to be more sensitive to the body's own antigens. Immune responses to one's own tissues can result in the degeneration of the tissues and may be responsible for such conditions as arthritic joint disorders, chronic glomerulonephritis, and hyperthyroidism. In addition, T lymphocytes tend to lose their functional capacity with aging and cannot destroy abnormal cells, such as cancer cells, as efficiently. This change may be one reason that certain types of cancer occur more frequently in older people.

One of the greatest disadvantages of aging is the increasing lack of ability to adjust to stress. Homeostasis is far more precarious in elderly people, and eventually the body encounters some stressor so great that the body's ability to recover is surpassed and death results.

Death

Death is usually not attributed to old age. Some other problem, such as heart failure, renal failure, or stroke, is usually listed as the cause of death.

Death was once defined as the loss of heartbeat and respiration. In recent years, however, more precise definitions of death have been developed because both the heart and the lungs can be kept working artificially, as occurs during cardiopulmonary resuscitation, and the heart can even be temporarily replaced by an artificial device. Modern definitions of death are based on the permanent cessation of life functions and the cessation of integrated tissue and organ function. The most widely accepted indication of death in humans is whole brain death, which is manifested clinically by the absence of (1) response to stimulation, (2) natural respiration and heart function, and (3) brainstem reflexes, in addition to an electroencephalogram (EEG) that remains isoelectric ("flat") for at least 30 minutes.

When determining death, certain conditions also need to be ruled out. For example, some central nervous system poisons can cause a flat EEG, but the patient can be revived if the effects of the poison are eliminated. Hypothermia slows all chemical reactions, including those involved in degenerative changes that begin at the time of death. As a result, a person suffering from hypothermia can exhibit no response to stimulation, exhibit no respiration or heartbeat, and have a flat EEG for more than 30 minutes and still be revived.

Neocortical (nee-oh-KOR-ti-kal) **death** is a condition in which major portions of the cerebrum are no longer functioning. The patient is comatose and incapable of responding to stimuli. However, heartbeat and respiration still continue because of some relatively unimpaired brainstem functions. Also, because some brainstem function remains, the EEG is not flat but exhibits some level of activity. Under these conditions, some state laws require that the patient be kept alive by intravenous feeding and by other support equipment. The patient may have previously stated in a living will that, if neocortical death occurs and he or she cannot be returned to a reasonably normal level of function, no artificial support should be applied in an attempt to keep the body alive.

20.7 GENETICS

Learning Outcomes *After reading this section, you should be able to*

A. Define genetics, and explain how chromosomes are related to inheritance.
B. Describe the major types of inheritance.

Genetics is the study of heredity—that is, the characteristics children inherit from their parents. Many of a person's characteristics, including specific abilities, susceptibility to certain diseases, and even lifespan, are influenced by heredity. The functional units of heredity are **genes,** which are carried on chromosomes.

Chromosomes

Deoxyribonucleic (dee-OCK-see-RYE-boh-noo-KLEE-ik) **acid (DNA)** molecules and their associated proteins become visible as densely stained bodies, called **mitotic chromosomes** (KROH-moh-sohmz), during cell division (see chapter 3). **Somatic** (soh-MAT-ik) **cells,** all the cells of the body except the reproductive cells, contain 23 pairs of chromosomes, or 46 total chromosomes. The reproductive cells, or **gametes** (GAM-eets), contain 23 unpaired chromosomes.

A **karyotype** (KAR-ee-oh-type) is a display of the chromosomes in a somatic cell (figure 20.19; see chapter 3). There are 22 pairs of **autosomes,** which are all the chromosomes except the sex chromosomes, and there is one pair of **sex chromosomes.** The sex chromosome pair of a normal female consists of two **X chromosomes** (XX) in each somatic cell, whereas the sex chromosome pair of a normal male consists of one X and one **Y chromosome** (XY).

Figure 20.19 **Human Karyotype**

The 23 pairs of chromosomes in humans consist of 22 pairs of autosomes (numbered 1–22) and 1 pair of sex chromosomes. The autosome pairs are numbered in order from largest to smallest. This is the karyotype of a male, as evidenced by the presence of an X and a Y sex chromosome. A female karyotype would have 2 X chromosomes.

CNRI/Science Source

Gametes are produced by **meiosis** (my-OH-sis) (see chapter 19). Meiosis is called a reduction division because it produces gametes that have half the number of chromosomes that somatic cells have. When a sperm cell and a secondary oocyte fuse during fertilization, each contributes one-half of the chromosomes necessary to produce new somatic cells. Therefore, half of an individual's genetic makeup comes from the father, and half comes from the mother.

During meiosis, the chromosomes are distributed in such a way that each gamete receives only one chromosome from each **homologous** (ho-MOL-oh-gus) pair of chromosomes (see chapter 19). Homologous chromosomes contain the same complement of genetic information. The determination of sex illustrates, in part, how chromosomes are distributed during gamete formation and fertilization. During meiosis and gamete formation, the pair of sex chromosomes separates, so that each secondary oocyte receives one X chromosome, whereas each sperm cell receives either an X chromosome or a Y chromosome (figure 20.20). When a sperm cell fertilizes an oocyte to form a zygote, the genetic sex of the individual is determined randomly. If the oocyte is fertilized by a sperm cell with a Y chromosome the zygote is genetically male; if the oocyte is fertilized by a sperm cell with an X chromosome, the zygote is genetically a female. Estimating the probability that any given zygote will be male or female is much like flipping a coin. For any given fertilization event, there is a 50% probability that the individual will be genetically female and 50% probability that the individual will be genetically male.

Figure 20.20 **Inheritance of Sex**

The female produces oocytes containing one X chromosome, whereas the male produces sperm cells with either an X or a Y chromosome. There are four possible combinations of an oocyte with a sperm cell, half of which produce females and half of which produce males.

Genes

Each chromosome contains thousands of genes. Each **gene** consists of a certain portion of a DNA molecule, but not necessarily a continuous stretch of DNA. Genes determine the proteins in a cell. Both chromosomes of a given pair contain similar but not necessarily identical genes. Similar genes on homologous chromosomes are called **alleles** (a-leelz). If the two allelic genes are identical, the person is **homozygous** (ho-moh-ZY-gus) for the trait specified by that gene. If the two alleles are slightly different, the person is **heterozygous** (HET-er-oh-ZY-gus) for the trait. All the genes in one homologous set of 23 chromosomes in one individual constitute that person's **genome** (jee-nohm).

Through the processes of meiosis, gamete formation, and fertilization, the distribution of genes received from each parent is essentially random. This random distribution is influenced by several factors, however. First, all the genes on a given chromosome are **linked;** that is, they tend to be inherited as a set rather than as individual genes because chromosomes, not individual genes, segregate during meiosis. Second, homologous chromosomes may exchange genetic information during meiosis by **crossing over.**

Segregation errors may occur during meiosis. As the chromosomes separate, the two members of a homologous pair may not segregate. As a result, one of the daughter cells receives both chromosomes of a given pair, and the other daughter cell receives none. When the gametes are fertilized, the

resulting zygote has either 47 chromosomes or 45 chromosomes, rather than the normal 46. When this condition results in an abnormal autosomal chromosome number, it is usually, but not always, lethal and is one reason for a high rate of early embryo loss. **Down syndrome,** or *trisomy 21,* which results when there are three copies of chromosome 21, is one of the few autosomal trisomies that is not lethal. In contrast, sex chromosome abnormalities are not usually lethal. For example, **Turner Syndrome** or *monosomy X,* in which only one X chromosome is present, results in sterility and abnormal sexual development but does not affect the mental development of the female.

Dominant and Recessive Genes

Most human genetic traits are recognized because defective alleles for those traits exist in the population. For example, on chromosome 11 is a gene that produces an enzyme necessary for the synthesis of melanin, the pigment responsible for skin, hair, and eye color (see chapter 5). An abnormal allele, however, produces a defective enzyme not capable of catalyzing one of the steps in melanin synthesis. If a given person inherits two defective alleles, a homozygous condition, the person is unable to produce melanin and therefore lacks normal pigment. This condition is referred to as **albinism** (AL-bi-nizm).

For many genetic traits, the effects of one allele for that trait can mask the effect of another allele for the same trait. For example, a person who is heterozygous for the melanin-producing enzyme gene has one normal gene for melanin production and one defective gene for melanin production. One copy of the gene and its resulting enzymes are enough to make normal melanin. As a result, the person who is heterozygous produces melanin and appears normal. In this case, the allele that produces the normal enzyme is said to be **dominant,** whereas the allele producing the abnormal enzyme is **recessive.** By convention, dominant traits are indicated by uppercase letters, and recessive traits are indicated by lowercase letters. In this example, the letter *A* designates the dominant normal, pigmented allele, and the letter *a* designates the recessive abnormal allele. Not all dominant traits are the normal condition, and not all recessive traits are abnormal. Many examples exist of abnormal dominant traits. For example, **Huntington disease,** a degenerative neurological disease, is caused by an abnormal dominant gene.

When analyzing the possible gene combinations to explain certain genetic traits, the use of letters to represent the alleles becomes very helpful. For example, the possible combinations of dominant and recessive alleles for normal melanin production versus albinism are *AA* (homozygous dominant, normal), *Aa* (heterozygous, normal), and *aa* (homozygous recessive, albino). The combination of alleles a person has for a given trait is called the **genotype** (JEN-oh-type). The person's appearance is called the **phenotype** (FEE-noh-type). A person with the genotype *AA* or *Aa* has the phenotype of normal pigmentation, whereas a person with the genotype *aa* has the phenotype of albinism. The recessive trait is expressed only when no allele for the dominant trait is present. A **carrier** is a heterozygous person with an abnormal recessive gene but a normal phenotype because the normal dominant allele for that gene is also present.

Apply It 5

Polydactyly *(pol-ee-DAK-ti-lee) is the condition of having extra fingers or toes. Given that polydactyly is a dominant trait, list all the possible genotypes and phenotypes for polydactyly. Use the letters D and d for the alleles.*

The inheritance of dominant and recessive traits can be determined if the genotypes of the parents are known. For example, if an albino person (*aa*) mates with a heterozygous normal person (*Aa*), the probability that the child will be albino (*aa*) is one-half, and the probability that the child will be normal (*Aa*) is one-half. If two carriers (*Aa*) mate, the probability that the child will be homozygous dominant (*AA*) or homozygous recessive (*aa*) is one-fourth for either genotype. The probability that the child will be heterozygous (*Aa*) is one-half. Such a probability can be determined easily by using a table called a **Punnett square** (figure 20.21).

Figure 20.21 **Inheritance of a Recessive Trait: Albinism**

A represents the normal pigmented condition, and *a* represents the recessive unpigmented condition. This Punnett square represents a mating between two normal carriers.

Sex-Linked Traits

Traits affected by genes on the sex chromosomes are called **sex-linked traits.** Most sex-linked traits are **X-linked;** that is, they are on the X chromosome. Only a few **Y-linked** traits exist, largely because the Y chromosome is very small. An example of an X-linked trait is **hemophilia A** (classic hemophilia), in which the person is unable to produce one of the clotting factors (see chapter 11). Consequently, clotting is impaired, and persistent bleeding can occur, either spontaneously or as a result of an injury. Hemophilia A is a recessive trait, and the allele for the trait is located on the X chromosome. The possible genotypes and phenotypes are therefore

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X^HX^H (normal homozygous female)
X^HX^h (normal heterozygous female)
X^hX^h (hemophiliac homozygous female)
X^HY (normal male)
X^hY (hemophiliac male)

Note that a female must have both recessive alleles to exhibit hemophilia, whereas a male has hemophilia if he has one recessive allele, because he has only one X chromosome. A Punnett square representing the inheritance of hemophilia is illustrated in figure 20.22. If a female who is a carrier for hemophilia mates with a male who does not have hemophilia, none of their daughters will have hemophilia; however, the probability that a son will have hemophilia is one-half. On the other hand, the probability that a daughter will be a carrier is one-half.

Figure 20.22 **Inheritance of an X-Linked Trait: Hemophilia**
X^H represents the normal X chromosome condition with all clotting factors, and X^h represents the X chromosome lacking an allele for one clotting factor. This Punnett square represents a mating between a normal male and a normal carrier female.

Apply It 6

What is the probability that a female with Turner Syndrome will have hemophilia if her mother is a carrier for hemophilia?

Other Types of Gene Expression

In some cases, the dominant allele does not completely mask the effects of the recessive allele. This is called **incomplete dominance.** An example of incomplete dominance is **sickle-cell anemia,** in which the hemoglobin produced by the gene is abnormal. The result is sickle-shaped red blood cells, which are likely to stick in capillaries and tend to rupture more easily than normal red blood cells. The normal hemoglobin allele (*S*) is dominant over the sickle-cell allele (*s*). A normal person (*SS*) has normal hemoglobin, and a person with sickle-cell anemia (*ss*) has abnormal hemoglobin. A person who is heterozygous (*Ss*) has half normal hemoglobin and half abnormal hemoglobin and usually has only a few sickle-shaped red blood cells. This condition is called **sickle-cell trait.**

In another type of gene expression, called **codominance** (koh-DOM-ih-nans), two alleles can combine to produce an effect without either of them being dominant or recessive. For example, a person with type AB blood has A antigens and B antigens on the surface of his or her red blood cells (see chapter 11). The antigens result from a gene that causes the production of the A antigen and a different gene that causes the production of the B antigen, and neither gene is dominant or recessive in relation to the other.

Many traits, called **polygenic** (pol-ee-JEN-ik) **traits,** are determined by the expression of multiple genes on different chromosomes. Examples are height, intelligence, eye color, and skin color. Polygenic traits typically have a great amount of variability. For example, there are many shades of eye color and skin color (figure 20.23).

Figure 20.23 **Inheritance of a Polygenic Trait: Skin Color**

This example shows three genes for skin color. Each of the dominant alleles (*A, B, C*) contributes one "unit of dark color" to the offspring (indicated by a *dark dot*). Each of the recessive alleles (*a, b, c*) contributes one "unit of light color" to the offspring (indicated by a *light dot*). The dominant alleles are incompletely dominant over the recessive alleles. (*a*) In a mating between a very light-skinned person (*aabbcc*) and a very dark-skinned person (*AABBCC*), all the offspring are of intermediate color. (*b*) In a mating between two people of intermediate skin color (*AaBbCc*), a very low percentage of the offspring (less than 2%) are either very light or very dark, and most are of intermediate color.

Genetic Disorders

Genetic disorders are caused by abnormalities in a person's genetic makeup—that is, in his or her DNA. They may involve a single gene or an entire chromosome. Some genetic disorders result from a **mutation** (myoo-TAY-shun; to change), a change in a gene that usually involves a change in the nucleotides composing the DNA (see chapter 2). Mutations occur by chance or can be caused by chemicals, radiation, or viruses. If mutations occur in reproductive cells, abnormal traits resulting from these mutations can be passed from one generation to the next.

The importance of genes is dramatically illustrated by situations in which the alteration of a single gene results in a genetic disorder. For example, in **phenylketonuria** (FEN-il-KEE-toh-NYOO-ree-ah) **(PKU),** the gene responsible for producing an enzyme that converts the amino acid phenylalanine to the amino acid tyrosine is defective. Therefore, phenylalanine accumulates in the blood and is eventually converted to harmful substances that can cause mental retardation.

Genetic Counseling

Genetic counseling includes predicting the possible results of matings involving carriers of harmful genes and talking to parents or prospective parents about the possible outcomes and treatments of a genetic disorder. With this knowledge, prospective parents can make informed decisions about having children.

The first step in genetic counseling is to attempt to determine the genotype of the individuals involved. A family tree, or **pedigree,** provides historical information about family members. Figure 20.24 shows the pedigree for a simple dominant trait, such as Huntington disease, a neurological disorder. Sometimes, knowing the phenotypes of relatives makes it possible to determine a person's genotype. As part of the process of collecting information, a karyotype can be prepared. For some genetic disorders, the amount of a given substance, such as an enzyme, produced by a carrier can be tested. For example, carriers for cystic fibrosis produce more salt in their sweat than is normal.

Figure 20.24 **Pedigree of a Simple Dominant Trait**

Males are indicated by *squares*, females by *circles*. People who express the trait are indicated in *purple*. The *horizontal line* between symbols represents a mating. The symbols connected to the mating line by *vertical* and *horizontal lines* represent the children resulting from the mating in order of birth from left to right. Matings not related to the pedigree are not shown.

TABLE 20.3 REPRESENTATIVE DISEASES AND DISORDERS: Pregnancy

Condition	Description
Ectopic pregnancy	Pregnancy that occurs outside the uterus, usually in the uterine tube; as the pregnancy progresses, the tube ruptures, which may lead to life-threatening internal bleeding
Miscarriage	Death or early delivery of the fetus; approximately 15% of all pregnancies end in miscarriage
Placenta previa	The placenta implants near the opening of the uterus in the cervical canal; as the fetus grows and the uterus stretches, the placenta may tear away from the uterine wall, resulting in death of the fetus; associated hemorrhaging can be life-threatening to the mother as well.
Toxemia (tok-SEE-mee-ah) (pregnancy-induced hypertension)	Increased blood pressure associated with pregnancy; may result in convulsions, kidney failure, and death of both the mother and fetus
Teratogens (TER-ah-toh-jenz)	Drugs or other chemicals that can cross the placenta and cause birth defects in the developing embryo; for example, thalidomide (tha-LID-o-myde) causes abnormal limb development
Fetal alcohol syndrome (FAS)	Brain dysfunction, impaired growth, and facial peculiarities in children of women who consumed substantial amounts of alcohol while pregnant
Infections	
Rubella (German measles)	If rubella is contracted by a pregnant female, the fetus may be severely affected; results include visual and hearing defects as well as cognitive disability.
Neonatal gonorrheal ophthalmia	Severe form of conjunctivitis contracted by an infant passing through the birth canal of a mother infected with gonorrhea; carries a high risk of blindness; can be prevented by treating a newborn's eye with silver nitrate and antibiotics

Condition	Description
Chlamydial conjunctivitis	Contracted by an infant passing through the birth canal of a mother infected with chlamydia
Human immunodeficiency virus (HIV)	Virus that causes acquired immunodeficiency syndrome (AIDS); can infect the fetus in utero, during parturition, or during breastfeeding; the drug azidothymidine (AZT) inhibits HIV replication and can reduce the number of infants who contract AIDS if given to HIV-infected pregnant women and to their newborn infants

SUMMARY

20.1 Prenatal Development

1. The eight stages of life are germinal period (fertilization to 14 days); embryo (14–56 days after fertilization); fetus (56 days after fertilization to birth); neonate (birth–1 month); infant (1 month–1 or 2 years); child (1 or 2 years–puberty); adolescent (puberty–20 years); adult (20 years–death).
2. Prenatal development is an important part of an individual's life. About 3 of every 100 people are born with a birth defect requiring early medical attention.
3. The developing human is called an embryo during the first 8 weeks of the prenatal period and a fetus from 8 weeks until birth.
4. Developmental age is 14 days less than clinical age.

Fertilization

Fertilization, the union of the secondary oocyte and sperm cell, results in a zygote.

Early Cell Division

The zygote undergoes divisions until it becomes a mass of cells.

Blastocyst

1. The embryonic mass develops a cavity and is known as the blastocyst.
2. The blastocyst consists of a trophoblast and an inner cell mass, where the embryo forms.

Implantation of the Blastocyst and Development of the Placenta

1. The blastocyst implants in the uterus about 7 days after fertilization.
2. The embryonic portion of the placenta is derived from the trophoblast of the blastocyst.

Maternal Hormonal Changes

1. Human chorionic gonadotropin levels are high in early pregnancy but then decline to low levels.
2. Progesterone and estrogen levels are low in early pregnancy but increase to high levels late in pregnancy.

Formation of the Germ Layers

1. The embryo forms around the primitive streak, which forms about 14 days after fertilization.
2. All tissues of the body are derived from the three primary germ layers: ectoderm, mesoderm, and endoderm.

Neural Tube and Neural Crest Formation

The nervous system develops from a neural tube that forms in the ectodermal surface of the embryo and from neural crest cells derived from the developing neural tube.

Formation of the General Body Structure

1. The limbs develop as outgrowths called limb buds.
2. The face develops by fusion of five tissue masses.

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Development of the Organ Systems

1. The digestive tract develops as the developing embryo closes off part of the yolk sac.
2. The heart develops as two blood vessels fuse into a single tube that develops septa to form four chambers.
3. The kidneys and the reproductive system are closely related in their development.

Growth of the Fetus

During the fetal period, the fetus increases 15-fold in length and 1400-fold in weight.

20.2 Parturition

1. Uterine contractions force the baby out of the uterus during labor.
2. Increased estrogen, decreased progesterone, and secretions from the fetal adrenal cortex initiate parturition.
3. Stretching of the uterus stimulates oxytocin secretion, which stimulates uterine contractions.

20.3 The Newborn

Respiratory and Circulatory Changes

1. Inflation of the lungs at birth results in closure of the foramen ovale and the ductus arteriosus.
2. When the umbilical cord is cut, blood no longer flows through the umbilical vessels.

Digestive Changes

The digestive system only gradually develops the ability to digest a variety of foods.

20.4 Lactation

1. Estrogen and progesterone help stimulate the growth of the breasts during pregnancy.
2. Suckling stimulates prolactin and oxytocin synthesis. Prolactin stimulates milk production, and oxytocin stimulates milk letdown.

20.5 First Year Following Birth

Many of the important changes that occur during the first year after birth are linked to continued development of the brain.

20.6 Life Stages

The Aging Process

1. Aging occurs as irreplaceable cells wear out and the tissue becomes more brittle and less able to repair damage.
2. Atherosclerosis is the deposit of lipids in the arteries. Arteriosclerosis is hardening of the arteries.

Death

Death is defined as the absence of brain response to stimulation, the absence of natural respiration and heart function, and a flat electroencephalogram for 30 minutes.

20.7 Genetics

Chromosomes

1. Humans have 46 chromosomes in 23 pairs.
2. Males have the sex chromosomes XY, and females have XX.
3. During gamete formation, the chromosomes of each pair of chromosomes separate; therefore, half of a person's genetic makeup comes from the father and half from the mother.

Genes

1. A gene is a portion of a DNA molecule. Genes determine the proteins in a cell.
2. Genes are paired (located on the paired chromosomes).
3. Dominant genes mask the effects of recessive genes.
4. Sex-linked traits result from genes on the sex chromosomes.
5. In incomplete dominance, the heterozygote expresses a trait that is intermediate between the two homozygous traits.
6. In codominance, neither gene is dominant or recessive, but both are fully expressed.
7. Polygenic traits result from the expression of multiple genes.

Genetic Disorders

1. A mutation is a change in the DNA.
2. Some genetic disorders result from an abnormal distribution of chromosomes during gamete formation.

Genetic Counseling

1. A pedigree (family history) can be used to determine the risk of having children with a genetic disorder.
2. Specific chemical tests or an examination of a person's karyotype can be used to determine a person's genotype.

REMEMBERING AND UNDERSTANDING

1. Define clinical age and developmental age, and state the difference between the two in number of days. Define embryo and fetus.
2. What are the events during the first week after fertilization? Define zygote, morula, and blastocyst.
3. How does the placenta develop?
4. Describe the formation of the germ layers and the role of the primitive streak.
5. How are the neural tube and neural crest cells formed? What do they become?
6. Describe the formation of the limbs and face.
7. Describe the formation of the digestive tract.
8. How does the single heart tube become four-chambered?
9. What major events distinguish embryonic and fetal development?

10. Describe the hormonal changes that take place before and during parturition.
11. What changes take place in the newborn's circulatory system and digestive system shortly after birth?
12. What hormones are involved in preparing the breasts for lactation? What hormones are involved in milk production and milk letdown?
13. Describe the changes in motor and language skills that take place during the first year of life.
14. List the different life stages.
15. How does the loss of cells that are not replaced affect the aging process? Give examples.
16. How does the loss of tissue elasticity affect the aging process? Give examples.

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17. How does aging affect the immune system?
18. Define death.
19. Give the number and type of chromosomes in the karyotype of a human somatic cell. How do the chromosomes of a male and a female differ from each other?
20. How do the chromosomes in somatic cells and gametes differ from each other?
21. What is a gene, and how are genes responsible for the structure and function of cells?
22. Define homozygous dominant, heterozygous, and homozygous recessive.
23. What is a sex-linked trait? Give an example.
24. How do sickle-cell anemia, type AB blood, and a person's height result from the expression of genes?
25. What is a mutation?
26. What is the cause of the genetic disorder Down syndrome?
27. How are pedigrees, karyotypes, and chemical tests used in genetic counseling?

CRITICAL THINKING

1. A physician tells a woman that her pregnancy has progressed 44 days since her last menstrual period (LMP). How many days has the embryo been developing, and what developmental events are occurring?
2. A high fever can prevent neural tube closure. If a woman has a high fever about 35 to 45 days post-LMP, what kinds of birth defects may be seen in the developing embryo?
3. A drug that stops the production of milk in the breast after a few days probably has which effect?
   a. inhibits prolactin secretion
   b. inhibits oxytocin secretion
   c. increases estrogen secretion
   d. increases progesterone secretion
   e. increases prolactin secretion
4. Dimpled cheeks are inherited as a dominant trait. Is it possible for two parents, each of whom has dimpled cheeks, to have a child without dimpled cheeks? Explain.
5. The ability to roll the tongue to form a "tube" results from a dominant gene. Suppose that a woman and her son can both roll their tongues, but her husband cannot. Is it possible to determine if the husband is the father of her son based on this trait?
6. A woman who does not have hemophilia marries a man who has the disorder. Determine the genotypes of both parents if they have a daughter with hemophilia.

Answers to this chapter's odd-numbered critical thinking questions appear in Appendix D

Design Elements: (Microbes in Your Body): Janice Haney Carr/CDC; (Clinical Impact): Comstock/Alamy Stock Photo

Appendix A

Table of Measurements

TABLE A.1 Table of Measurements

Unit	Metric Equivalent	Symbol	U.S. Equivalent
Measures of Length			
1 kilometer	= 1000 meters	km	0.62137 mile
1 meter	= 10 decimeters or 100 centimeters	m	39.37 inches
1 decimeter	= 10 centimeters	dm	3.937 inches
1 centimeter	= 10 millimeters	cm	0.3937 inch
1 millimeter	= 1000 micrometers	mm	
1 micrometer[a]	= 1/1000 millimeter or 1000 nanometers	µm	
1 nanometer[a]	= 10 angstroms or 1000 picometers	nm	No U.S. equivalent
1 angstrom	= 1/10,000,000 millimeter	Å	
1 picometer	= 1/1,000,000,000 millimeter	pm	
Measures of Volume			
1 cubic meter	= 1000 cubic decimeters	m^3	1.308 cubic yards
1 cubic decimeter	= 1000 cubic centimeters	dm^3	0.03531 cubic foot
1 cubic centimeter	= 1000 cubic millimeters or 1 milliliter	cm^3 (cc)	0.06102 cubic inch
Measures of Capacity			
1 kiloliter	= 1000 liters	kL	264.18 gallons
1 liter	= 10 deciliters	L	1.0567 quarts
1 deciliter	= 100 milliliters	dL	0.4227 cup
1 milliliter	= volume of 1 gram of water at standard temperature and pressure	mL	0.3381 ounce

Unit	Metric Equivalent	Symbol	U.S. Equivalent
1 microliter	= 1 mm^3 (cubic millimeter) or 10^{-6} L	μL	
Measures of Mass			
1 kilogram	= 1000 grams	kg	2.2046 pounds
1 gram	= 100 centigrams or 1000 milligrams	g	0.0353 ounce
1 centigram	= 10 milligrams	cg	0.1543 grain
1 milligram	= 1/1000 gram	mg	

[a]A micrometer was formerly called a micron (μm), and a nanometer was formerly called a millimicron (mμ).

TABLE A.2 Comparative Temperature Scales

Appendix B

Some Reference Laboratory Values

TABLE B.1	Blood, Plasma, or Serum Values	
Test	**Normal Values**	**Clinical Significance**
Acetoacetate plus acetone	0.32-2 mg/100 mL	Values increase in diabetic acidosis, fasting, high-fat diet, and toxemia of pregnancy.
Ammonia	9-33 µmol/L (micromol/L)	Values decrease with proteinuria and as a result of severe burns; values increase in multiple myeloma.
Amylase	4-25 U/mL[a]	Values increase in acute pancreatitis, intestinal obstruction, and mumps; values decrease in cirrhosis of the liver, toxemia of pregnancy, and chronic pancreatitis.
Barbiturate	0	Coma level: phenobarbital, approximately 10 mg/100 mL; most other drugs, 1-3 mg/100 mL.

Test	Normal Values	Clinical Significance
Bilirubin	0.4 mg/100 mL	Values increase in conditions causing red blood cell destruction, biliary obstruction, or liver inflammation.
Blood volume	8.5-9% of body weight in kilograms	
Calcium	8.5-10.5 mg/100 mL	Values increase in hyperparathyroidism, vitamin D hypervitaminosis; values decrease in hypoparathyroidism, malnutrition, and severe diarrhea.
Carbon dioxide content	24-30 mEq/L[b] 20-26 mEq/L in infants (as HCO_3^-)	Values increase in respiratory diseases, vomiting, and intestinal obstruction; values decrease in acidosis, nephritis, and diarrhea.
Carbon monoxide	0	Symptoms with over 20% saturation
Chloride	100-106 mEq/L	Values increase in Cushing syndrome, nephritis, and hyperventilation; values decrease in diabetic acidosis, Addison disease, and diarrhea, and also after severe burns.
Creatine phosphokinase (CPK)	Female: 5-35 mU/mL Male: 5-55 mU/mL	Values increase in myocardial infarction and skeletal muscle diseases, such as muscular dystrophy.
Creatinine	0.6-1.5 mg/100 mL	Values increase in certain kidney diseases.

Test	Normal Values	Clinical Significance
Ethanol	0	0.3-0.4%, marked intoxication 0.4-0.5%, alcoholic stupor Over 0.5%, alcoholic coma
Glucose	Fasting 70-110 mg/100 mL	Values increase in diabetes mellitus, liver diseases, nephritis, hyperthyroidism, and pregnancy; values decrease in hyperinsulinism, hypothyroidism, and Addison disease.
Iron	50-150 µg/100 mL	Values increase in various anemias and liver disease; values decrease in iron-deficiency anemia.
Lactic acid	0.6-1.8 mEq/L	Values increase with muscular activity and in congestive heart failure, severe hemorrhage, shock, and anaerobic exercise.
Lactic dehydrogenase	60-120 U/mL	Values increase in pernicious anemia, myocardial infarction, liver diseases, acute leukemia, and widespread carcinoma.

Test	Normal Values	Clinical Significance
Lipids	Cholesterol 120-220 mg/100 mL; cholesterol esters 60-75% of cholesterol; phospholipids 9-16 mg/100 mL as lipid phosphorus; total fatty acids 190-420 mg/100 mL Total lipids 450-1000 mg/100 mL Triglycerides 40-150 mg/100 mL	Increased values for cholesterol and triglycerides are connected with increased risk of cardiovascular disease, such as heart attack and stroke.
Lithium	Toxic levels 2 mEq/L	
Osmolality	285-295 mOsm/kg water	
Oxygen saturation (arterial) (see Po_2)	96-100%	
Pco_2	35-43 mm Hg	Values decrease in acidosis, nephritis, and diarrhea; values increase in respiratory diseases, intestinal obstruction, and vomiting.
pH	7.35-7.45	Values decrease as a result of hypoventilation, severe diarrhea, Addison disease, and diabetic acidosis; values increase due to hyperventilation, Cushing syndrome, and vomiting.
Po_2	75-100 mm Hg (breathing room air)	Values increase in polycythemia and decrease in anemia and obstructive pulmonary diseases.

Test	Normal Values	Clinical Significance
Phosphatase (acid)	Male: total 0.13-0.63 U/mL Female: total 0.01-0.56 U/mL	Values increase in cancer of the prostate gland, hyperparathyroidism, some liver diseases, myocardial infarction, and pulmonary embolism.
Phosphatase (alkaline)	13-39 IU/L[c] (infants and adolescents up to 104 IU/L)	Values increase in hyperparathyroidism, some liver diseases, and pregnancy.
Phosphorus (inorganic)	3-4.5 mg/100 mL (infants in first year up to 6 mg/100 mL)	Values increase in hypoparathyroidism, acromegaly, vitamin D hypervitaminosis, and kidney diseases; values decrease in hyperparathyroidism.
Potassium	3.5-5 mEq/100 mL	
Protein	Total 6-8.4 g/100 mL Albumin 3.5-5 g/100 mL Globulin 2.3-3.5 g/100 mL	Total protein values increase in severe dehydration and shock; values decrease in severe malnutrition and hemorrhage.
Salicylate Therapeutic Toxic	0	20-25 mg/100 mL Over 30 mg/100 mL Over 20 mg/100 mL after age 60
Sodium	135-145 mEq/L	Values increase in nephritis and severe dehydration; values decrease in Addison disease, myxedema, kidney disease, and diarrhea.
Sulfonamide Therapeutic	0	5-15 mg/100 mL

Test	Normal Values	Clinical Significance
Urea nitrogen	8-25 mg/100 mL	Values increase in response to increased dietary protein intake; values decrease in impaired renal function.
Uric acid	3-7 mg/100 mL	Values increase in gout and toxemia of pregnancy and as a result of tissue damage.

[c]A unit (U) is the quantity of a substance that has a physiological effect.

[b]A milliequivalent (mEq) is defined in Appendix C.

[c]A unit (U) is the quantity of a substance that has a physiological effect.

TABLE B.2 Blood Count Values

Test	Normal Values	Clinical Significance
Clotting (coagulation) time	5-10 min	Values increase in afibrinogenemia and hyperheparinemia, severe liver damage.
Hematocrit	Male: 40-54% Female: 38-47%	Values increase in polycythemia, severe dehydration, and shock; values decrease in anemia, leukemia, cirrhosis, and hyperthyroidism.
Fetal hemoglobin	Newborns: 60-90% Before age 2: 0-4% Adults: 0-2%	Values increase in thalassemia, sickle-cell anemia, and leakage of fetal blood into maternal bloodstream during pregnancy.

Test	Normal Values	Clinical Significance
Hemoglobin	Male: 14-16.5 g/100 mL Female: 12-15 g/100 mL Newborn: 14-20 g/100 mL	Values decrease in anemia, hyperthyroidism, cirrhosis of the liver, and severe hemorrhage; values increase in polycythemia, congestive heart failure, and obstructive pulmonary disease and at high altitude.
Ketone bodies	0.3-2 mg/100 mL Toxic level: 20 mg/100 mL	Values increase in ketoacidosis, fever, anorexia, fasting, starvation, and a high-fat diet.
Platelet count	250,000-400,000/μL	Values decrease in anemias and allergic conditions and during cancer chemotherapy; values increase in cancer, trauma, heart disease, and cirrhosis.
Prothrombin time	11-15 s	Values increase in prothrombin and vitamin deficiency, liver disease, and hypervitaminosis A.
Red blood cell count	Males: 4.6-6.2 million/μL Females: 4.2-5.4 million/μL	Values decrease in systemic lupus erythematosus, anemias, and Addison disease; values increase in polycythemia and dehydration and following hemorrhage.
Reticulocyte count	1-3%	Values decrease in iron-deficiency and pernicious anemias and radiation therapy; values increase in hemolytic anemia, leukemia, and metastatic carcinoma.

Test	Normal Values	Clinical Significance
White blood cell count, differential	Neutrophils 60-70% Eosinophils 2-4% Basophils 0.5-1% Lymphocytes 20-25% Monocytes 3-8%	Neutrophils increase in acute infections; eosinophils and basophils increase in allergic reactions; monocytes increase in chronic infections; lymphocytes increase during antigen-antibody reactions.
White blood cell count, total	5000-9000/ µL	Values decrease in diabetes mellitus, anemias, and following cancer chemotherapy; values increase in acute infections, trauma, some malignant diseases, and some cardiovascular diseases.

TABLE B.3 Urine Values

Test	Normal Values	Clinical Significance
Acetone and acetoacetate	0	Values increase in diabetic acidosis and during fasting.
Albumin	0 to trace	Values increase in glomerular nephritis and hypertension.
Ammonia	20-70 mEq/L	Values increase in diabetes mellitus and liver disease.
Bacterial count	Under 10,000/mL	Values increase in urinary tract infection.
Bile and bilirubin	0	Values increase in biliary tract obstruction.
Calcium	Under 250 mg/24 h	Values increase in hyperparathyroidism and decrease in hypoparathyroidism.
Chloride	110-254 mEq/24 h	Values decrease in pyloric obstruction and diarrhea; values increase in Addison disease and dehydration.

Test	Normal Values	Clinical Significance
Potassium	25-100 mEq/L	Values decrease in diarrhea, malabsorption syndrome, and adrenal cortical insufficiency; values increase in chronic renal failure, dehydration, and Cushing syndrome.
Sodium	75-200 mg/24 h	Values decrease in diarrhea, acute renal failure, and Cushing syndrome; values increase in dehydration, starvation, and diabetic acidosis.
Creatinine clearance	100-140 mL/min	Values increase in renal diseases.
Creatinine	1-2 g/24 h	Values increase in infections and decrease in muscular atrophy, anemia, and certain kidney diseases.
Glucose	0	Values increase in diabetes mellitus and certain pituitary gland disorders.
Urea clearance	Over 40 mL of blood cleared of urea per min	Values increase in certain kidney diseases.
Urea	25-35 g/24 h	Values decrease in complete biliary obstruction and severe diarrhea; values increase in liver diseases and hemolytic anemia.
Uric acid	0.6-1 g/24 h	Values increase in gout and decrease in certain kidney diseases.
Casts		
Epithelial	Occasional	Values increase in nephrosis and heavy metal poisoning.
Granular	Occasional	Values increase in nephritis and pyelonephritis.
Hyaline	Occasional	Values increase in glomerular membrane damage and fever.

Test	Normal Values	Clinical Significance
Red blood cell	Occasional	Values increase in pyelonephritis; blood cells appear in urine in response to kidney stones and cystitis.
White blood cell	Occasional	Values increase in kidney infections.
Color	Amber, straw, transparent yellow	Color varies with hydration, diet, and disease states.
Odor	Aromatic	Odor becomes acetone-like in diabetic ketosis.
Osmolality	500-800 mOsm/kg water	Values decrease in aldosteronism and diabetes insipidus; values increase in high-protein diets, heart failure, and dehydration.
pH	4.6-8	Values decrease in acidosis, emphysema, starvation, and dehydration; values increase in urinary tract infections and severe alkalosis.

TABLE B.4 Hormone Levels

Test	Normal Values
Steroid hormones	
Aldosterone	Excretion: 5-19 µg/24 h[a]
Fasting, at rest, 210 mEq sodium diet	Supine: 48 ± 29 pg/mL[b]
	Upright: 65 ± 23 pg/mL
Fasting, at rest, 10 mEq sodium diet	Supine: 175 ± 75 pg/mL
	Upright: 532 ± 228 pg/mL
Cortisol	
Fasting	8 am: 5-25 µg/100 mL
At rest	8 pm: Below 10 µg/100 mL

Test	Normal Values
Testosterone	Adult male: 300-1100 ng/100 mL[c] Adolescent male: over 100 ng/100 mL Female: 25-90 ng/100 mL
Peptide hormones	
Adrenocorticotropin (ACTH)	15-170 pg/mL
Calcitonin	Undetectable in normal individuals
Growth hormone (GH)	
Fasting, at rest	Below 5 ng/mL
After exercise	Children: over 10 ng/mL Male: below 5 ng/mL Female: up to 30 ng/mL
Insulin	
Fasting	6-26 μU/mL
During hypoglycemia	Below 20 μU/mL
After glucose	Up to 150 μU/mL
Luteinizing hormone (LH)	Male: 6-18 mU/mL Preovulatory or postovulatory female: 5-22 mU/mL Midcycle peak 30-250 mU/mL
Parathyroid hormone	Less than 10 μEq/L[d]
Prolactin	2-15 ng/mL
Renin activity	
Normal diet	
Supine	1.1 Â± 0.8 ng/mL/h
Upright	1.9 Â± 1.7 ng/mL/h
Low-sodium diet	
Supine	2.7 Â± 1.8 ng/mL/h
Upright	6.6 Â± 2.5 ng/mL/h
Thyroid-stimulating hormone (TSH)	0.5-3.5 μU/mL
Thyroxine-binding globulin	15.25 μg T_4/100 mL
Total thyroxine	4-12 μg/100 mL

Test	Normal Values

[a]1 microgram (1 µg) is equal to 10^{-6} g.
[b]1 picogram (1 pg) is equal to 10^{-12} g.
[c]1 nanogram (1 ng) is equal to 10^{-9} g.
[d]µEq microequivalent, 1/1000 mEq, which is defined in Appendix C.

Appendix C

Answers to Process Figure Questions

Chapter 1

Process Figure 1.1 First, consider the definition of an organ: An organ is a structure that is composed of at least two types of tissue. Because the skin consists of both epithelial and connective tissues, it fits the definition of an organ. The integumentary system is composed of the skin and other small organs, such as sweat glands and sebaceous glands. The combination of these organs constitutes an organ system: a group of organs with a common function.

Process Figure 1.4 All homeostatic mechanisms are regulated by feedback. All three components of a homeostatic mechanism are necessary to keep body variables within their normal range. There are multiple points at which the mechanism may break down. (1) If the receptors are not functioning, then the stimulus cannot be detected and no response will be initiated. In this example, if the body temperature receptors have become insensitive to high temperatures, then they wouldn't send a signal to the control center and the temperature would rise. (2) If the control center does not receive the receptors' signal or is insensitive to the receptors' input, then it will not send a message to the effector. If the control center allows the body temperature to rise much higher than normal without stimulating the sweat glands, then the person would not sweat when they became too hot. (3) If the effector does not work properly, it cannot carry out the response that will return the body to the set point. If the sweat glands are not functioning and do not secrete sweat, the body is not capable of cooling down as effectively as when sweat is produced, and the person could suffer heat stroke.

Chapter 2

Process Figure 2.4 First, recall that covalent bonds are formed when atoms share electrons, while ionic bonds are formed when atoms transfer electrons. Now, with that in mind, because the question stated that electrons are shared, you know that it must be a covalent bond, not an ionic bond. The next point to remember is that an atom with higher electronegativity will attract electrons more strongly than an atom with weak electronegativity, so that there will be unequal sharing of electrons. This tells you that the covalent bond must be a polar bond, because equal sharing of electrons results in a nonpolar covalent bond.

Chapter 3

Process Figure 3.3 Recall from chapter 2 that a change in temperature is related to a similar change in molecular motion. An increase in temperature would increase molecular motion, thereby speeding up the diffusion of the salt crystals. A decrease in temperature would decrease molecular motion, thereby slowing the rate of salt crystal diffusion.

Process Figure 3.4 The information in the question states that aldosterone determines the transport of Na^+ out of the urine and into the blood. If a person with Addison disease lacks sufficient levels of aldosterone, Na^+ levels in the urine would be higher than normal. Because water will move to areas with higher solute concentrations, we can also conclude that urine volume would be higher than normal, because water diffuses from the blood into urine, similar to the movement of water from the beaker into the tube.

Process Figure 3.8 Recall that carrier-mediated transport mechanisms demonstrate specificity. The carrier molecule represented in this figure transports glucose. Different carrier molecules specific to certain amino acids would be necessary for amino acid transport.

Process Figure 3.10 The cell is "paying" the energy cost through the use of ATP. Recall that the sodium-potassium pump is an active transport mechanism that requires ATP to move Na^+ and K^+ across the membrane. As such, the cell's energy cost is "paid" during the first step of the figure.

Process Figure 3.11 Receptor proteins demonstrate specificity. As a result of this specificity, the cell regulates what can bind to the receptors and therefore what is transported into the cell.

Process Figure 3.12 Recall that exocytosis is a form of vesicular transport that allows cells to release substances that are often too large to be transported by carrier molecules. Exocytosis is a form of bulk transport allowing for the movement of many substances at the same time.

Process Figure 3.15 From the figure we can see that ribosomal subunits are composed of ribosomal RNA (rRNA) and ribosomal proteins. Recall from chapter 2 that RNA is composed of nucleotides and proteins are composed of amino acids.

Process Figure 3.18 The digestive enzymes are isolated in the lysosomes to prevent the digestion of the normal parts of the cell.

Process Figure 3.22 As shown in the figure, transcription occurs in the nucleus and translation occurs in the cytoplasm, in association with ribosomes. Recall that our cells have membrane-bound nuclei and the nuclear envelope separates the contents of the nucleus from the cytoplasm. As a result, transcription must be completed before the mRNA molecule can exit the nucleus and enter the cytoplasm. Only then can the mRNA interact with the ribosome to complete the translation process. Bacterial cells do not have membrane-bound nuclei, so the ribosomes can associate with the forming mRNA before the process of transcription is completed.

Process Figure 3.23 Recall that each nucleotide of nucleic acids is composed of a sugar, a base, and a phosphate group. RNA nucleotides have ribose sugar, thus the name *ribonucleic acid*. DNA nucleotides have deoxyribose sugar, thus the name *deoxyribonucleic acids*.

Process Figure 3.25 We know that the process of mitosis produces daughter cells with exactly the same DNA as the parent and therefore exactly the same diploid number. The information provided suggests that one cell is lacking a chromosome (45) and one cell has an extra chromosome (47). It appears that the

chromatids of a chromosome did not separate correctly and both moved into one new cell. Because the separation of chromatids occurs during anaphase, we can conclude that this is where the error occurred.

Chapter 4

Process Figure 4.7 The characteristics of inflammation (redness, swelling, etc.) are due to increased blood flow to the site of injury. While it is very important to bring more blood to the injury site to provide more oxygen to the different cells as well as to increase the number of white blood cells, sometimes the inflammation response can become detrimental. RICE helps control the amount of blood arriving at the injured location. Rest reduces activity of the tissues so less oxygen is needed. Ice causes vasoconstriction, which reduces blood flow, and compression aids in moving excess fluid away from the area. Finally, elevation uses the force of gravity to aid in drawing fluid from the area. This is useful in recovery because excess swelling can actually prevent oxygen and nutrient delivery and can cause more damage than the original injury.

Process Figure 4.8 Recall from chapter 3 that the cellular division process called mitosis creates new cells. In preparation for mitosis, existing cells copy their DNA and then during mitosis each cell separates into two new, identical cells. This increases the total number of cells in an area. Mitosis creates cells to fill in the gap in the epidermis created by an injury.

Chapter 5

Process Figure 5.4 DNA is primarily located in the nucleus. But recall that mitochondria also contain DNA. We can assume that the melanosomes would congregate around the structures that contain DNA—the nucleus and possibly the mitochondria.

Process Figure 5.9 Blood flows through the skin to release heat but also to ensure that the temperature of the skin is maintained at a homeostatic level. As the skin temperature drops due to the placement of the ice pack, blood vessels in that area will dilate to increase blood flow and therefore heat at the site.

Chapter 6

Process Figure 6.5 Recall from chapter 3 that cellular material is released in bulk by exocytosis. Thus, osteoblasts release the materials for bone matrix production by exocytosis.

Process Figure 6.6 We learned that osteoclasts are bone-destroying cells. Next, we're told that the osteoclasts remove the calcified cartilage from the centers of ossification. The most likely mechanism for this is phagocytosis. Large cells that work to remove or destroy wastes do so, in part, through this type of endocytosis.

Process Figure 6.7 Looking at figure 6.7, we can see that the mechanism promoting long bone growth is division of chondrocytes. This cell division increases the amount of hyaline cartilage in the epiphyseal plate, which makes the overall bone length greater. Therefore, the major effect of GH is to stimulate chondrocyte cell division.

Process Figure 6.8 To answer this question, first recall stimuli for bone remodeling. One of the major promoters of bone remodeling and increased bone thickness is mechanical stress on the bone. Astronauts in very low gravity do not experience as much stress on their bones as do people living on Earth with its gravitational pull. Because there is less mechanical stimulation of osteoblasts, you would expect bones to heal more slowly in astronauts living in the international space station without the normal pull of gravity.

Chapter 7

Process Figure 7.6 This is facilitated diffusion. Recall from chapter 3 that movement of a molecule or ion down its concentration gradient is a type of passive transport, specifically diffusion if the molecule or ion is a solute. However, diffusion of ions cannot occur directly through the phospholipid bilayer. Thus, a transport protein is required to "help" along the diffusion of the molecule or ion.

Process Figure 7.7 You learned that the charge on the inside of the membrane of an electrically excitable cell is negative (below zero). You also learned that K^+ is in higher concentration inside the cell membrane and constantly diffuses out of the cell through K^+ leak channels. Negatively charged proteins inside the cell cannot diffuse through the cell membrane. In a cell that has a greater number of K^+ leak channels, the permeability of the membrane to K^+ is greater and more K^+ than normal will diffuse out of the cell. The negatively charged proteins left behind will cause the charge inside the cell to become even more negative. With the inside more negative, the resting membrane potential will be farther from zero.

Process Figure 7.8 To answer this question, recall that the neuromuscular junction is the structure where skeletal muscle contractions are stimulated. The neurotransmitter acetylcholine binds to acetylcholine receptors on the sarcolemma. Without acetylcholine receptors, no signal for contraction will be transmitted to the muscle fiber and skeletal muscles would remain flaccid (not contracted). Giving the patient an acetylcholinesterase inhibitor is effective because it prevents degradation of acetylcholine in the synaptic cleft. By keeping the concentration of acetylcholine elevated, the limited number of receptors will be stimulated to a greater degree.

Process Figure 7.9 First, an action potential in a motor neuron results in acetylcholine release. In turn, the acetylcholine binds to

acetylcholine-gated Na^+ channels, allowing Na^+ to diffuse into the muscle fiber. If not enough Na^+ enters to reach the threshold of the sarcolemma, no action potential will be generated. Without an action potential traveling down the T tubules, there is no Ca^{2+} released from the sarcoplasmic reticulum. Calcium ions are required to expose the myosin attachment sites, so if no Ca^{2+} is released, there will not be a contraction in the muscle fiber.

Process Figure 7.10 The question tells you that Ca^{2+} diffuses out of the sarcoplasmic reticulum after a person dies. Because the myosin heads are in their resting position in a relaxed muscle, the presence of Ca^{2+} will cause the myosin heads to automatically engage the actin myofilaments and the muscle will contract. However, ATP production ceases upon the death of a person. You learned that ATP is required for two steps in the cross-bridge cycle: (1) Detachment of the myosin head and (2) returning the myosin head to its resting position. Thus, the absence of ATP in a corpse prevents the release of already formed cross-bridges and the muscles stay rigid. Rigor mortis does not happen in a living person because during life ATP does not get completely depleted. However, it can be significantly reduced when muscles have been overworked. In the case of severely overworked muscles, there is still enough ATP to allow a few cross-bridges to form, resulting in a weak contraction. However, there are not enough cross-bridges formed to allow a person to stand or walk.

Process Figure 7.13 You learned that ATP production is continuous during exercise. However, you also learned that ATP consumption can outpace ATP production. If that happens, the myosin heads have a reduced capacity to reset and very little Ca^{2+} is pumped back into the sarcoplasmic reticulum. Thus, after severe physical activity, a muscle may be unable to form sufficient cross-bridges to support standing or walking. This is different than when rigor mortis occurs upon a person's death. In rigor mortis, there is a complete lack of ATP and cross-bridge release is not possible.

Chapter 8

Process Figure 8.7 Ions are charged atoms or molecules. The charge of ions will affect the direction of movement because opposite charges are attracted to each other and same charges are repelled from each other. We learned that the inside surface of the cell membrane is slightly negative. Because Cl^- are also negative, we can conclude that the negative charge inside the cell repels the Cl^-, thereby reducing the number of Cl^- that enter the cell.

Process Figure 8.8 Sodium ions are moving down the concentration gradient in this figure, by diffusion. Recall from chapter 3 that diffusion is a passive process.

Process Figure 8.9 The process is active. In figure 8.7 we learned that the sodium-potassium pump functions to maintain the differential levels of Na^+ and K^+ across the cell membrane. This membrane protein is an active transport mechanism, requiring ATP to transport the ions from one side of the membrane to the other.

Process Figure 8.12 The ion channel that is depicted is a chemically-gated channel. Opening of these channels leads to local potential. Action potentials result from the opening of voltage-gated channels.

Process Figure 8.16 Recall that the motor division of the PNS is divided into the somatic nervous system, which controls skeletal muscle tissue, and the autonomic nervous system, which controls cardiac and smooth muscle and glands. The reflex example in this figure is a somatic reflex because the effector is skeletal muscle.

Process Figure 8.17 The result we want for this particular reflex is for the upper limb to bend or flex. To determine this, we just need to identify the flexor muscles of the upper limb. By reviewing the muscles described in table 7.14 we can see that the biceps brachii and the brachialis are the flexor muscles; therefore, these are the

muscles that must be stretched to initiate the reflex to flex or bend the arm.

Process Figure 8.18 Remember that stretch reflexes are stimulated by stretching of a muscle. During the withdrawal reflex, as the flexor muscles contract, the extensor muscles are stretching. The inhibition overrides the normal response of these muscles to contract and allows for the coordinated movement of the limb.

Process Figure 8.30 The athletic trainer's conclusion is sensible considering the function of the cerebellum. Recall that the cerebellum ensures smooth and coordinated muscle contractions. The jerky, exaggerated movements exhibited by the kicker may be an indication of cerebellar damage. A thorough exam by a trained physician is needed to verify this, so the athletic trainer was accurate to insist that the player be transported to a hospital.

Process Figure 8.35 If production levels of CSF are normal, accumulation of CSF would result from issues with the movement and drainage of CSF into the venous system. We can conclude that either flow of CSF within the brain is blocked or issues with the veins that drain the CSF from the brain tissue are abnormal.

Chapter 9

Process Figure 9.13 Recall from chapter 8 that action potentials occur when ions move across cell membranes. Steps 2 and 3 both involve the generation of action potentials, so both involve ion movement across cell membranes.

Process Figure 9.16 Recall from chapter 3 that mitochondria are the primary location for ATP production in the cell. In step 5 of this figure we can see that ATP is needed for the recombination of rhodopsin molecules, which are necessary for the normal function of photoreceptors. We can hypothesize that mitochondrial diseases reduce normal ATP levels and therefore reduce the recycling of rhodopsin molecules in the photoreceptors.

Process Figure 9.18 Before answering the question, review part (a) of the figure. Notice the color-coding of the visual fields and the indicated areas of the visual pathways associated with each. If a lesion occurred in the left optic nerve just prior to the optic chiasm, action potentials from the left eyeball would be blocked completely. This essentially causes blindness in the left eye. If the lesion occurs in the visual pathway posterior to the optic chiasm, then action potentials are still conducted to the brain from both eyeballs, but not from the entire visual field. Just past the optic chiasm, we find axons carrying signals from the nasal part of the left visual field (dark green) and the temporal part of the right visual field (light blue). A lesion in this area would therefore interrupt signals associated with these regions, resulting in an incomplete image from both eyes.

Process Figure 9.22 Remember that the middle ear is normally an air-filled space. If fluid accumulated in the middle ear, the auditory ossicles would not be able to move as easily. The auditory ossicles transmit vibrations of the tympanic membrane to the oval window, and therefore into the inner ear. If they cannot move as easily, the vibrations would not be conducted as accurately to the

inner ear, resulting in less stimulation of the hair cells. Essentially, the accumulated fluid reduces the conduction of sound waves toward the inner ear.

Process Figure 9.23 Cochlear implants function by detecting sounds and stimulating the cochlear nerve. This type of device works well for individuals that suffer from conduction deafness. If a person has sensorineural hearing loss due to damage of the cochlear nerve, stimulating it artificially most likely will not alleviate the hearing loss.

Chapter 10

Process Figure 10.4 Recall from chapter 3 that the cell membrane contains embedded membrane proteins. These membrane proteins provide many functions of the cell. The cell functions include membrane transport or, in this example, response to a chemical messenger. Chemical messengers, including neurotransmitters, must bind to a membrane protein—specifically, a receptor—in order to communicate with their target cell. Once the neurotransmitter binds to its receptor, the binding triggers a specific sequence of events in the cell.

Process Figure 10.5 You learned that there are three ways to regulate hormone secretion by endocrine cells: humoral stimuli, neural stimuli, and hormonal stimuli. Process figure 10.5 shows hormonal stimuli for hormone secretion. In step 1, a hormone from the hypothalamus binds to receptors on particular endocrine cells of the anterior pituitary. The hypothalamic hormone then stimulates the anterior pituitary cell to secrete a specific hormone.

Process Figure 10.6 First, define humoral stimulus. A humoral stimulus is stimulation of the secretion of a hormone by a blood-borne chemical, such as glucose or Ca^{2+}. Levels of the chemical in the blood regulate the hormone's secretion. For example, high blood levels of glucose stimulate insulin secretion. Insulin stimulates cells to take up glucose, lowering blood levels back to the normal range. The lower levels of blood glucose inhibit further insulin secretion. In other words, blood levels of glucose provide a negative-feedback signal for reduced insulin secretion.

Process Figure 10.9 To answer this question, you need to relate the solubility of a molecule to the ability of that molecule to cross cell membranes. You learned that lipid-soluble hormones can easily cross cell membranes. Once the hormones are inside the cell, they

bind to intracellular receptors and stimulate a response. Because anabolic steroids are lipid-soluble hormones, they can enter any cell in the body. If the cell has a receptor with which the anabolic steroid can interact, the cell can be regulated by it.

Process Figure 10.10 Activation of the G protein stimulates the enzyme adenylate cyclase to produce cAMP. Once sufficient levels of cAMP are produced, the enzyme phosphodiesterase inactivates cAMP. If phosphodiesterase is not active, levels of cAMP will rise. Because caffeine is a stimulant, we can conclude that one mechanism of caffeine is to inhibit phosphodiesterase, preventing break down of cAMP.

Process Figure 10.13 You learned in section 10.6 that a certain hormone is synthesized by a specific cell type and that each hormone must bind to a specific receptor in order to generate its response. In order to respond independently to hypothalamic hormones, each cell type of the anterior pituitary must possess a unique receptor for its specific hypothalamic-releasing hormone.

Process Figure 10.14 To answer this question, first recall that the two posterior pituitary hormones are synthesized by neurons whose cell bodies are in the hypothalamus. The hormones are stored in membrane-bound vesicles in the axon terminals, which are located in the posterior pituitary. Because the posterior pituitary hormones are stored in vesicles, they must be water-soluble hormones—lipid-soluble hormones would simply diffuse out of the vesicles.

Process Figure 10.19 Epinephrine and norepinephrine from the adrenal medulla and sympathetic neurons have the same chemical composition; they differ simply in the way they arrive at their target. When secreted by the adrenal medulla, epinephrine and norepinephrine are called hormones because they travel in the blood to their targets. Epinephrine and norepinephrine secreted by sympathetic neurons are called neurotransmitters because they are secreted into a synapse directly onto their targets.

Process Figure 10.20 Because cortisol suppresses the immune system, prescription of the related cortisone or other similar drugs is useful to reduce the inflammatory and immune responses. These drugs are often given to reduce inflammation caused by joint injuries. Cortisone can also reduce the immune and inflammatory responses that result from allergic reactions or abnormal immune responses, such as rheumatoid arthritis or asthma.

Chapter 11

Process Figure 11.7 One of the products of hemoglobin breakdown is bilirubin. Bilirubin is secreted into the small intestine as part of bile and eventually excreted as part of feces. Bilirubin derivatives contribute to the color of feces. A person that is suffering from anemia due to fewer, smaller red blood cells would excrete less bilirubin; therefore the color of the feces would be affected.

Process Figure 11.10 In step 2 we see that thromboxane is one of the chemical signals that activate platelets. Without platelet activation, platelet plug formation will not occur.

Process Figure 11.11 Stage 1 is the most likely answer. If hemophilia affects clotting factors, then those clotting factors could not activate prothrombinase. Therefore, stages 2 and 3 would not occur.

Process Figure 11.14 In this case, the fetus would be capable of producing the anti-Rh antibodies. Remember that the fetal blood and maternal blood are in separate circulations and the mixing of blood usually occurs later in the pregnancy. The production of anti-Rh antibodies in the fetus would not pose a threat to the fetus and would not be sufficient to pose a threat to the mother during the pregnancy.

Chapter 12

Process Figure 12.10 The first question refers only to the pulmonary circulation. Remember that the right side of the heart pumps blood into the pulmonary circulation. Starting in the right atrium, a red blood cell will pass through the tricuspid valve into the right ventricle and then through the pulmonary semilunar valve into the pulmonary trunk. From the pulmonary trunk, blood flows to the lungs. So for the first question, the answer is 2 (tricuspid and pulmonary semilunar valve). The second question refers to the systemic circulation. The left side of the heart pumps blood to the systemic circulations, but remember, we are starting in the right atrium in this scenario as well. Blood returning from the lungs passes from the left atrium through the bicuspid into the left ventricle and then through the aortic semilunar valve into the aorta. Blood is then distributed to the different systems, including the brain. So we include the tricuspid and pulmonary semilunar valves from the right side as well as the bicuspid and aortic semilunar valve from the left side, for a total of 4.

Process Figure 12.14 Recall that an atrioventricular valve is located between an atrium and a ventricle; therefore, it regulates blood movement from the atrium into the ventricle. This is described in step 3. A semilunar valve is located between a ventricle and a great artery, regulating blood movement from the ventricle into the great artery. This is described in step 5.

Process Figure 12.16 Blood flows from the ventricles to the great vessels, which are located superiorly, at the base of the heart. Contraction of the ventricles from the apex to the base moves the blood toward the great vessels. Similar to squeezing a toothpaste tube from the crimped end toward the opening, contraction of the ventricles from the apex toward the base empties the ventricles more effectively.

Process Figure 12.18 From the figure we can see that ventricular systole includes steps 3 and 4. Also, the question states that isovolumetric means "same volume." In step 3 the ventricles are contracting but the AV valves and semilunar valves are closed. Blood is not moving during this time of ventricular contraction, so the volume in the ventricles remains the same. We can conclude that the isovolumetric phase occurs at the beginning of ventricular systole when all valves are closed. In step 4, the semilunar valves are forced open and blood flows into the pulmonary trunk and aorta. This would be the ventricular ejection phase, given that blood is forced or ejected from the ventricles.

Process Figure 12.23 As you can see from this figure, the sympathetic and parasympathetic divisions influence heart rate by increasing or decreasing it from the rate established by the SA node. Meditation is a method that is purported to reduce emotional excitement and stress, thereby reducing sympathetic stimulation of the heart.

Chapter 13

Process Figure 13.17 Recall that the brachial artery branches at the elbow, forming the radial and ulnar artery. When blood flow is blocked through the brachial artery, blood flow will also be reduced in these two arteries.

Process Figure 13.20 A high-sodium diet results in a higher concentration of sodium in the blood and therefore a higher osmotic pressure. This higher osmotic pressure would reduce the net movement of fluid out of the capillary at the arterial end of the capillary and increase the net movement of fluid into the capillary at the venous end. Overall, there would be a higher fluid volume in the blood vessels, resulting in higher blood pressure overall.

Process Figure 13.22 When you are sleeping, skeletal muscle activity is low, and therefore the buildup of metabolic by-products is low. In addition, the tissues need less O_2 and fewer nutrients. Based on these points, we can conclude that condition 2, when precapillary sphincters are contracted and blood flow is reduced, would exist in skeletal muscle of a sleeping individual.

Process Figure 13.23 Based on the name, step 3 is most likely involved. Parasympathetic stimulation via the vagus nerve decreases heart rate and therefore blood pressure. The sudden drop in blood pressure leads to a lack of blood flow to the brain, and fainting can occur. The vasovagal response also decreases sympathetic stimulation (steps 4 and 5), further influencing a drop in blood pressure.

Process Figure 13.25 Holding your breath leads to an increase in blood CO_2 and a decrease in pH. These chemical changes would lead to increased sympathetic stimulation that would increase heart rate, stroke volume, and vasoconstriction, all of which would lead to an increase in blood pressure.

Process Figure 13.26 The release of epinephrine by the adrenal medulla increases stimulation of the heart, thereby increasing heart rate and stroke volume. Epinephrine also causes vasoconstriction of many blood vessels. If a person were injected with epinephrine, we would expect the same responses, all of which would increase blood pressure.

Process Figure 13.27 The answer to this question is simply osmosis. Remember that water moves from areas of low solute concentration to areas of higher solute concentration. As more Na^+ is reabsorbed at the kidneys, water will follow the solute and be absorbed as well.

Chapter 14

Process Figure 14.7 It seems simple, but this is a point that many students forget. The lymph nodes and spleen differ as to which body fluid they filter. The lymph nodes filter debris and pathogens from lymph before it is returned to the blood. The spleen filters debris, worn-out red blood cells, and pathogens from blood.

Process Figure 14.11 In table 10.1 we can see that autocrine communication involves the release of chemical messengers that bind to receptors on the secreting cell. In this figure, that type of communication occurs at step 4 as the helper T cell releases Interleukin-2 that then binds to Interleukin-2 receptors on the same helper T cell. Paracrine communication involves the release of chemical messengers that bind to receptors on neighboring cells. This type of communication occurs in step 3 as the macrophage releases Interleukin-1 that binds Interleukin-1 receptors on the helper T cell.

Process Figure 14.12 Recall that proteins are produced at ribosomes. Also, these proteins will be released from the cell, which requires that they be packaged in vesicles for secretion. In this case, we can assume that plasma cells will have ample rough endoplasmic reticulum, as this is the site of protein synthesis for secreted proteins, as well as ample Golgi apparatuses for packaging the antibodies into secretory vesicles.

Process Figure 14.15 Memory cells are the key to secondary responses. Memory cells allow for a faster and greater response to a specific antigen. The presence of memory cells allows for a faster response because these cells do not have to go through the same number of steps (interacting with helper T cells) to produce plasma cells. Also, the presence of memory cells increases the actual number of cells specific to the antigen; therefore there are more immune cells responding to the antigen in the secondary response compared to the primary response.

Process Figure 14.16 There are several differences that can be identified when comparing the events in this figure to the events in figure 14.11. First, cytotoxic T cells respond to antigens on individual target cells, meaning those that are infected or mutated. Helper T cells respond to antigen displayed by antigen-presenting cells, which are other immune cells that have encountered the antigen. Next, cytotoxic T cells interact with MHC class I molecules on the target cell. This type of MHC molecules is present on most nucleated cells. Helper T cells interact with MHC class II molecules, which are associated with antigen-presenting cells. Finally, costimulation of cytotoxic T cells involves CD8 markers, whereas helper T cell costimulation involves CD4 markers.

Chapter 15

Process Figure 15.12 Airflow into the lungs is achieved by pressure differences. As step 2 indicates, inspiration occurs when the diaphragm contracts and the thoracic wall expands. These two events increase the volume in the thoracic cavity, which lowers the pressure there. If atmospheric pressure is higher than alveolar pressure, air flows into the lungs. At higher altitudes, the atmospheric pressure is lower than at sea level. Thus, when a person inhales while at higher altitude, less air flows into the lungs. The reduced airflow per breath is what causes people to feel that the air is "thinner" at higher altitudes (see the Clinical Impact "Effects of High Altitude and Emphysema").

Process Figure 15.13 At the alveoli, CO_2 diffuses from the blood into the alveoli because the partial pressure of CO_2 is higher in the blood than in the alveoli. If a person breathed into and out of a paper bag, the PCO_2 in the bag would increase and less CO_2 would diffuse out of the person's blood due to a less steep partial pressure gradient. Eventually CO_2 levels in the blood would increase and the brain would adjust the breathing rate. This is why breathing into a paper bag is one way to control hyperventilation due to anxiety. Hyperventilation actually causes CO_2 levels to drop, so taking 6 to 12 normal breaths into and out of a paper bag helps return CO_2 levels to normal, which relieves hyperventilation.

Process Figure 15.15 The concentration of H^+ is the determinant of pH. Recall from chapter 2 that acidic pH is due to a high concentration of H^+. The pH of the red blood cell cytoplasm is maintained within the normal range in part by hemoglobin binding to H^+. If red blood cells had fewer hemoglobin molecules, as is the case with some forms of anemia, the concentration of H^+ not bound to hemoglobin would increase and the pH would become acidic. Hemoglobin serves as a pH buffer in the red blood cell cytoplasm.

Chapter 16

Process Figure 16.9 Certain viral infections, such as the common cold or the flu, cause inflammation of the oropharynx. Because the voluntary phase of the swallowing requires the tongue to push a bolus of food into the oropharynx, inflammation there shrinks the glottis, which means that a greater degree of muscle contraction is required to swallow an even smaller-than-normal-sized bolus. The pain associated with the inflammation of the pharynx also makes swallowing unpleasant.

Process Figure 16.10 If materials move through the digestive tract too quickly, there isn't enough time to absorb sufficient water from the chyme and it stays too liquid. Liquid feces is called diarrhea.

Process Figure 16.12 Stomach emptying takes 4 to 6 hours after a full meal. If the entire stomach contents were to enter the duodenum all at once, the enzymes and epithelial cells lining the small intestine would be overwhelmed. Not all of the nutrients would be processed or absorbed (see section 16.4, "Movement in the Stomach").

Process Figure 16.13 The longer stomach acid is in the stomach, the more likely it is to be forced back into the esophagus through the weakened gastroesophageal opening. Because it is the introduction of stomach acid into the esophagus that causes the symptoms of heartburn, a medication that slows stomach emptying could worsen heartburn symptoms. The medication may increase the chance that instead of the stomach acid entering the small intestine, it would be forced back into the esophagus. If untreated, prolonged exposure of the esophagus to stomach acid could cause esophageal ulcers or other disorders.

Process Figure 16.16 Because segmental contractions mix and disperse the chyme throughout the small intestine, there is more

surface area of the food exposed to digestive enzymes and the digested food is exposed to transport proteins on the intestinal epithelium. Without the segmental contractions, digestion and absorption would be reduced and malnourishment could eventually result.

Process Figure 16.18 If the gallstones become too large, they block the cystic duct, preventing bile from leaving the gallbladder. This can be very painful. Sometimes smaller gallstones migrate to the duodenal papilla and become lodged there, which also blocks pancreatic secretions from entering the duodenum. In each example, the digestive process is interfered with when secretions of the gallbladder or pancreas are blocked. For example, when such secretions are blocked, stomach acids are not diluted and neutralized to as great an extent as if bile were present. Lipids are not emulsified by the bile, which results in decreased lipid digestion and absorption. Excretory products, such as the bile pigments, cholesterol, and lipids, are not as readily removed from the body.

Process Figure 16.19 The principal function of cholecystokinin is to stimulate contractions of the gallbladder. Contractions of the gallbladder send a burst of bile into the duodenum. If the gallbladder is absent, this cannot happen. Doctors often recommend a low-fat diet to patients whose gallbladder has been removed.

Process Figure 16.21 Because the secretion of cholecystokinin and secretin is regulated by nutrients in the duodenum and by parasympathetic nerves, a blockage to the pancreatic duct would not have an effect on cholecystokinin and secretin blood levels.

Process Figure 16.25 Movement of glucose into the intestinal epithelial cells is driven by Na^+ movement down its concentration gradient into the epithelial cell. Without the Na^+/K^+ pump continually moving Na^+ out of the intestinal cells to keep the concentration low, Na^+ levels would build up inside the cell. This

would destroy the necessary concentration gradient. Consequently, glucose absorption would be greatly reduced.

Process Figure 16.26 The lipids become surrounded with hydrophilic proteins inside the intestinal epithelial cells to form chylomicrons. Chylomicrons cannot move through the hydrophobic cell membrane by simple diffusion and are too large to move through a membrane transport protein. Consequently, they are packaged into vesicles for exocytosis across the plasma membrane and into lacteals.

Process Figure 16.28 Recall that the liver is the major metabolic center of the body. If the diet is lacking in certain types of amino acids, the liver can convert absorbed amino acids into the deficient ones. However, the liver cannot synthesize all necessary amino acids. Those amino acids that the liver cannot synthesize must be consumed in the diet.

Chapter 17

Process Figure 17.3 Anabolic reactions result in the synthesis of molecules such as proteins. In table 3.1, we can see that the site of protein synthesis is at ribosomes as well as in the rough endoplasmic reticulum. Lipid synthesis occurs in smooth endoplasmic reticulum.

Process Figure 17.4 Blocking glycolysis disrupts the breakdown of glucose. However, lipid and protein metabolism can still occur. Specifically, fatty acids of lipids and amino acids of proteins can be catabolized to produce ATP if glycolysis is disrupted.

Process Figure 17.6 Remember that a single glucose molecule is a 6-carbon molecule. The products of anaerobic respiration are lactic acid, NADH, and ATP. During the breakdown of glucose, only H atoms and electrons are transferred to ATP or NADH; the 6 carbons of glucose are distributed evenly into the lactic acid molecules. Hence, each lactic acid molecule has 3 carbon atoms.

Process Figure 17.7 The CO_2 produced by aerobic respiration is released from the cells and enters the blood. Recall from chapter 15 that CO_2 is transported in the blood as either dissolved gas, bound to hemoglobin within red blood cells, or converted to bicarbonate ions. Though bicarbonate ions are important buffers in the blood, eventually the CO_2 moves out of the blood and into the alveoli of the lungs, finally to be exhaled to the exterior of the body. That's something interesting to think about when you are eating your next candy bar.

Chapter 18

Process Figure 18.8 Osmosis is the driving force for water reabsorption. An increase in osmotic pressure would increase the rate of water movement into the blood from the kidney tubules. This would increase the total water reabsorbed.

Process Figure 18.9 You learned that there are three forces responsible for filtration: one outward force and two inward forces. If the inward forces were to exceed the outward force, no filtrate could be formed. If a person were to eat a high protein diet, levels of proteins in the blood would increase. The high-protein levels would increase one of the inward forces, the colloid osmotic pressure. With a higher colloid osmotic pressure, water in the Bowman capsule would be drawn back into the blood. Less filtrate would be formed, which would decrease the urine volume.

Process Figure 18.10 Recall from chapter 3 that microvilli dramatically increase the surface area of an epithelium. Thus, the epithelium in the proximal convoluted tubule can support the greater degree of reabsorption that occurs in that segment of the nephron compared to the other segments.

Process Figure 18.11 Because the descending limb of the loop of Henle is permeable to water, water moves out of the filtrate into the more concentrated interstitial fluid. The longer the loop of Henle, the more surface area there is to allow a greater degree of water conservation. Because water is not readily available to desert animals, being able to conserve the majority of water filtered out of the blood in the kidney is critical for their survival.

Process Figure 18.12 An important source of the high concentration of solutes in the interstitial fluid of the medulla is the active transport of Na^+ in the thick segment of the ascending limb of

the loop of Henle. If this active transport were prevented, the high concentration of solutes in the medulla would become depleted. Depletion of the medullary solutes would prevent the kidney from being able to conserve water.

Process Figure 18.13 By producing an excessive amount of filtrate, the blood is rapidly and repetitively filtered over the course of a day, which improves the efficiency of cleansing the blood and allows rapid removal of toxins. Reabsorption of nearly all of this filtered material is essential; otherwise we would soon have no blood at all.

Process Figure 18.19 Damage to sacral spinal nerves can result in an overactive or underactive urinary bladder, depending on the specific injury. An overactive urinary bladder causes frequent urination urges regardless of the urinary bladder fullness. In addition, urine may only dribble out of the urethra when urinating. An underactive urinary bladder causes a lack of urge to urinate even if the urinary bladder is completely full. In extreme cases, the urinary bladder may become so full that it bursts.

Chapter 19

Process Figure 19.2 Normally, each of the two cells undergoing anaphase II has 23 chromosomes. Each of the 23 chromosomes is present in two copies, or chromatids. If the chromatids don't separate during anaphase II, but instead migrate together, one cell will have one extra chromosome, or 24. The other cell will have one less chromosome, or 22.

Process Figure 19.5 The key to this question lies in the definition of a chromosome and how many copies of each chromosome exist during meiosis. Recall that prior to beginning meiosis, each chromosome is replicated such that a chromosome consists of two copies, called chromatids. Thus, although it states that each secondary spermatocyte has 23 chromosomes, each one exists in two copies. During meiosis II, it is the chromatids that separate. Thus, each spermatid has 23 chromosomes, each with only one copy.

Process Figure 19.7 You learned that testosterone has a negative-feedback effect on GnRH, LH, and FSH. If testosterone levels are higher than normal, we would expect the levels of GnRH, LH, and FSH to be lower than normal.

Process Figure 19.11 A secondary oocyte does not complete meiosis unless united with a sperm in fertilization. Thus, without sperm in the female reproductive tract, the secondary oocyte will exit the body during menstruation.

Chapter 20

Process Figure 20.2 Recall that each human sperm cell has 23 chromosomes. A human zygote normally has 46 chromosomes, 23 received from the sperm cell and 23 received from the oocyte. If two sperm cells fertilized the same secondary oocyte, the resulting zygote would have 69 chromosomes, 23 from the first sperm cell, 23 from the second sperm cell, and 23 from the oocyte (following the second meiotic division). An embryo fertilized by two sperm cells would not be viable, due to the abnormal amount of genetic material.

Process Figure 20.5 The secretion of hCG by the chorion ensures that the corpus luteum remains functional. Remember from chapter 19 that the corpus luteum degenerates if it is not stimulated by endocrine signals from the embryo. The secretion of progesterone and estrogen by the corpus luteum is important in the early stages of pregnancy to maintain the endometrial lining of the uterus. Without those signals, menses of the next menstrual cycle would begin and the embryo would be lost with the functional zone of the endometrium.

Process Figure 20.7 Though the embryonic disk changes from a two-layer structure to a three-layer structure, do not make the mistake of assuming that only one new layer of tissue develops. As you can see in steps 2 and 3 of this figure, the three embryonic layers (endoderm, mesoderm, and ectoderm) all are derived from the original ectoderm as a result of gastrulation. The hypoblast becomes part of the membranes around the developing embryo.

Process Figure 20.8 The notochord is a chord-like structure that forms from specialized cells of the primitive streak and delineates the central axis of the body. The neural tube is derived from ectoderm and gives rise to parts of the nervous system.

Process Figure 20.13 During the development of the interatrial septum, a hole normally exists that should close at birth. The interventricular septum, on the other hand, forms as a solid structure. Given that a hole is already present, it would be more likely that the existing hole does not close properly.

Process Figure 20.15 Recall that oxytocin is the hormone released by the posterior pituitary that stimulates uterine contractions. A synthetic form of oxytocin, known as Pitocin, is administered to women to enhance or even initiate labor contractions.

Process Figure 20.16 Progesterone has an inhibitory effect on the uterus. Estrogen, prostaglandins, and oxytocin all have stimulatory effects on the uterus.

Process Figure 20.17 Before birth, the umbilical veins carry oxygenated blood from the placenta to the fetus's circulation. Umbilical arteries carry deoxygenated blood from the fetus to the placenta. This is opposite of normal blood oxygenation levels after birth. Most arteries carry oxygenated blood and most veins carry deoxygenated blood. The exception to this pattern is in the pulmonary circulation, where pulmonary arteries carry deoxygenated blood from the heart to the lungs and pulmonary veins carry oxygenated blood from the lungs to the heart.

Process Figure 20.18 Recall that milk production occurs in mammary glands, specifically at the alveoli. Prolactin targets the secretory cells of the alveoli, stimulating increased milk production. The milk accumulates in the alveoli. Oxytocin stimulates smooth muscle cells that contract to expel the milk from the alveoli as well as smooth muscle cells that contract and move the milk through the lactiferous ducts of the mammary glands. Both hormones are needed so that milk production occurs (under the influence of prolactin) and so that the milk is released from the glands (under the influence of oxytocin).

Appendix D

Answers to Odd-Numbered Critical Thinking Questions

Chapter 1

1. To begin, let's examine why his body would be responding in this manner. Before the transfusion, his total blood volume was much lower than normal, due to the blood loss. The body attempts to compensate for less blood by increasing the heart rate, which usually increases blood pressure. However, there's not enough blood volume to do so. Thus, the heart rate continues to increase until the heart is beating so fast, it doesn't have time to fill with blood, which decreases blood pressure even further. This is an example of a harmful positive-feedback mechanism such that medical intervention (a transfusion) becomes necessary. Normally, increasing heart rate to increase blood pressure is successful and is an example of a common negative-feedback mechanism. In this case, however, it is inadequate to restore homeostasis. By giving the male a blood transfusion, his blood volume is brought back to a level at which normal blood pressure can be achieved.

3. To answer this question, recall the six characteristics of life: organization, metabolism, responsiveness, growth, development, and reproduction. Each of the first five is essential for life. For example, without organization, the human body would not exist in its hierarchical state, and structures that perform necessary life functions would not exist. However, reproduction occurs at the level of the cell or the organism. There are many people who never have offspring and live full, healthy lives. Thus, organismal reproduction is not essential to an individual's well-being. However, this is still a characteristic of life, because if all humans ceased to have offspring, the human population would eventually become extinct. Organismal reproduction is important at the population level.

5. Because the wedding band is being worn closer to the midline of the body, it should be worn proximal to the engagement ring.

7. Section 1.6, "Body Cavities" describes the distribution of organs among the three major body cavities. The text states that the reproductive organs, including the uterus (womb), are found in the pelvic cavity. The pelvic cavity contains the uterus, which increases

greatly in size during pregnancy as the fetus grows. However, the pelvic cavity is surrounded by bones, which are not expandable. Therefore, the uterus moves superiorly into the abdominal cavity, crowding abdominal organs and dramatically increasing the size of the abdominal cavity.

9. Look at figure 1.13. There you can see that although the kidneys are located in the abdominal cavity, they are retroperitoneal. In other words, they are posterior to the parietal peritoneum. When a person is lying prone, it is possible to cut through the posterior abdominal wall and remove a kidney without cutting through parietal peritoneum.

Chapter 2

1. Potassium and chlorine will form an ionic bond. To demonstrate this, draw the planetary models of potassium and chlorine:

   a. Now that you've drawn the planetary models, it is evident that K has only one electron in its valence shell, whereas Cl lacks only one to achieve an octet. Because K only has one electron, it is weakly electronegative. Because Cl only needs one electron, it is strongly electronegative. When two atoms of opposite electronegativities come together, the weak atom donates its electrons to the strong atom. In doing so, the atoms become ions with opposite charge. Oppositely charged ions are attracted to each other, forming an ionic bond.

3. To answer this question, it is helpful to remember that potential energy is stored energy, which humans acquire through food consumption. In order to build muscle mass, it is necessary to synthesize new proteins, the main component of muscle. The synthesis of molecules in living organisms results from chemical reactions that require the input of energy. The energy needed to drive these reactions comes from chemical reactions that release energy. The energy-releasing reactions occur when food molecules are broken down using decomposition reactions.

5. To explain the increase in heat, review the reaction of ATP breakdown in figure 2.8 as an example of a chemical reaction. When cells use ATP to do work, energy is released, some of which is released as heat. That's why during exercise, when cells are using more ATP, body temperature increases. In the example of warming the mixture of chemicals, the added heat functioned as activation energy to start a

chemical reaction. As you saw in figure 2.8, some of the energy released during breakdown of chemicals is released as heat. As a result of a chemical reaction and release of energy as heat, the solution became very hot.

Chapter 3

1. Before we draw a conclusion, let's think about an important piece of information provided: Grand Pacific Bay has a salt concentration slightly greater than that of human body fluids. That would mean that the Grand Pacific Bay is hypertonic compared to our body fluids. Recall that cells exposed to hypertonic solutions will lose water and shrink, not swell, as indicated by the autopsy. This allows us to eliminate A as a possibility. The fact that the cells of his lungs were swollen indicates that they were most likely exposed to a hypotonic solution, such as freshwater. Considering this, we can conclude that he probably drowned somewhere else and was placed in the bay. Although this is the most logical conclusion of those given, there are possibilities other than murder. For example, he may have accidentally drowned in a freshwater stream and then been washed into the bay.

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3. Because the plasma membrane stays the same size, even though small pieces of membrane from secretory vesicles are continually added to the plasma membrane, one must conclude that some process is removing small pieces of membrane at the same rate that they are added. The balance of adding new and removing old components of the cell membrane would allow the cell to remain the same size.

5. First, recall that a protein is composed of amino acids. The sequence of those amino acids is determined by a gene sequence. If a nucleotide is changed in the gene that specifies the protein, this could cause a change in the amino acid sequence as well. During transcription, the nucleotide sequence of a gene is transcribed into an mRNA molecule. Changing a nucleotide in the gene would also cause a change in the nucleotide sequence of the mRNA. During translation, codons of the mRNA determine the amino acid sequence of the protein. Changing the nucleotide sequence of the mRNA changed one of the codons, and therefore changed one of the amino acids. In chapter 2 we learned that the amino acid sequence determines the shape of the protein. As a result of the nucleotide change in DNA,

there was a change in the nucleotide sequence in the mRNA and a subsequent change in the amino acid sequence of the protein, ultimately changing the protein shape.

Chapter 4

1. You learned that pseudostratified ciliated columnar epithelium is normally found in the trachea. It produces mucus that traps dust and debris in the air. The cilia move the debris-containing mucus to the throat, where it is swallowed. However, you learned that in heavy smokers, the pseudostratified ciliated columnar epithelium is replaced by stratified squamous epithelium, which protects the trachea against smoke irritants. Because this type of epithelium is not ciliated, removal of foreign materials from the trachea is more difficult. After 2 years without smoking, the original pseudostratified ciliated columnar epithelium replaces the stratified squamous epithelium and debris removal resumes.

3. Generally, a secretory epithelium is a simple epithelium. Thus, there is only one cell layer in the enzyme-producing epithelium. To manufacture large amounts of enzymes, a cuboidal or columnar cell with the appropriate organelles, such as rough endoplasmic reticulum and a Golgi apparatus, would be expected. Therefore, we see that the secretory portion of the pancreas contains simple columnar epithelium. The columnar cells have microvilli on their free surface, which increase the surface area for secretion. The cells are held together by tight junctions. The tight junctions connect the epithelial cells of the pancreatic glands and duct system to each other. The tight junctions prevent damage from the pancreatic enzymes to the underlying tissues.

5. Because one of the main functions of the vertebral column in the back is to help us stand upright, the vertebrae need to be able to bend but then return to their original position (see chapter 6). The function of elastic fibers is to stretch and then spring back to their original shape. Connective tissue fibers are oriented in the direction in which connective tissue fibers can produce the strongest force. Thus, because the elastic fibers help to straighten the back after it has bent, the elastic fibers are organized parallel to the length of the ligaments between individual vertebrae.

7. Recall that histamine-induced inflammation results in vasodilation and increased permeability of blood vessels. These responses increase blood flow and white blood cell migration to a particular region, which allows the body to remove bacteria or other harmful agents. Taking an antihistamine would prevent this response and thus allow an infection to become worse. On the other hand, antihistamines also reduce many of the unpleasant symptoms of inflammation, making the patient more comfortable, and this is beneficial. Antihistamines are commonly taken to prevent allergy symptoms, which are often an overreaction of the inflammatory response to foreign substances, such as pollen or peanut dust.

Chapter 5

1. Recall that stretch marks occur when the skin is overstretched. This can be due to multiple factors, including rapid growth, obesity, and pregnancy. So, yes, it is possible for a woman who has never been pregnant to have stretch marks on her abdomen.

3. As stated in the question, the vermillion border is covered by keratinized epithelium that is a transition between the nonkeratinized stratified epithelium of the mucous membrane that covers the lips internally and the keratinized stratified epithelium of the facial skin. We learned in chapter 4 that a mucous membrane has mucous glands, which secrete mucus. The mucus helps keep the inner surface of the lips moist. In addition, the inner surface of the lips is "sealed off" most of the time and is moistened by saliva. In this chapter we learned that sebaceous or sweat glands are associated with normal skin, such as facial skin. The vermillion border lacks these glands. Without sebaceous glands, the surface of the vermillion border is not protected against drying by sebum. Also, the vermillion border is not as heavily keratinized as facial skin; that is, the number of cell layers with surrounding lipids is less. Consequently, the vermillion border dries out more easily.

5. Recall that acne is caused by the bacterium *Propionibacterium acnes*. As a consequence, several methods have some degree of success in treating acne: (1) Kill the bacteria. One effective agent is benzoyl peroxide in some acne medications. Antibiotics have also been used to treat severe cases of acne. (2) The lesions associated with acne are associated with overproduction of epidermal cells and accumulations of sebum. Another way to treat acne is to prevent sebum production. Isotretinoin, or Accutane (a derivative of vitamin A), has proven effective in preventing sebum production. However, Accutane produces birth defects and should be used with caution. Estrogen, a female sex hormone, has also been used to treat severe cases of acne. (3) The sebum accumulation results in the formation of a pimple, which may become infected. Another possible treatment is to unplug the follicle. Some sulfur compounds speed up peeling of the skin and unplug the follicle.

7. When first exposed to the cold temperature just before starting the run, we would expect the blood vessels in the skin constrict to conserve heat. This produces a pale skin color. Dilation of skin blood vessels does not occur at this time because the skin has not been exposed to the cold long enough to cause skin temperature to fall below 15°C (27°F). After running a while, as a result of the excess heat generated by the exercise, the blood vessels in the skin dilate. This results in heat loss and helps prevent overheating. Increased blood flow through the skin causes it to turn red. After the run, the body still has excess heat to eliminate, so for awhile the skin remains red.

Chapter 6

1. To answer this question, look at figure 6.7 and define epiphysis. The epiphysis is the site of new bone growth, because it houses the epiphyseal plate. Damage to the epiphyseal plate can result in a shortened limb. Because the injury separated the epiphysis from the diaphysis at the epiphyseal plate, the young male's femur did not grow as it normally would.

3. First, review the anatomy of the elbow joint: it consists of the radius and ulna articulating with the humerus. The ulna's olecranon process fits tightly into the posterior olecranon fossa of the humerus. On the other hand, the radius head is held near the capitulum of the humerus by ligaments. Thus, because the radius is not attached as tightly to the humerus as is the ulna, it is more likely that Samuel's radius pulled away from the humerus rather than his ulna.

5. The first task necessary to answer this question is to define osteoporosis. Osteoporosis is the depletion of bone matrix that results when more bone is destroyed than is formed. Second, recall bone remodeling and the stimuli that promote bone deposition. Because mechanical stress stimulates bone formation, primarily through activation of osteoblasts, running can help prevent, or slow, osteoporosis. This is true for the bones being stressed, which during running are the lower limb and spine.

Chapter 7

1. You learned that ATP is required for all skeletal muscle contraction. When Harrison was texting as fast as he could, his hands became fatigued due to ATP depletion. Without ATP, the muscles moving the fingers could not contract and his fingers could not flex or extend. The inability to release cross-bridges due to lack of ATP is called physiological contracture.

3. First, consider the actions of each group of muscles. Anterior arm muscles primarily flex the elbow, whereas posterior arm muscles primarily extend the elbow. Thus, the exercise that best builds the anterior arm muscles is flexion of the elbow against force, as in pull-ups. A pull-up with the hand supinated builds both the biceps and the brachialis, but a curl with the hand pronated builds the brachialis to a greater extent. The posterior arm is best built by extension of the elbow, as in push-ups or dips. Anterior forearm muscles primarily flex the fingers and wrist and pronate the forearm. The anterior forearm muscles are best built by forcefully flexing the wrist and fingers. Anterior thigh muscles primarily extend the knee and flex the hip. Thus, the anterior thigh muscles are best built by extending the knee, as in partial knee bends. Posterior leg muscles primarily flex the ankles and toes, and thus these are best built by standing on your toes. Abdominal muscles primarily flex the vertebral column and compress the abdomen. Therefore, the abdominal muscles are best built by flexing the vertebral column against resistance, as in leg lifts or partial sit-ups. Each exercise has to be repeated many times to increase the size of the muscles.

5. First, we are told that Javier suffered interruptions in functions under control of the muscular system (blurred vision, nausea, and spastic contractions). The fact that his muscles contracted without relaxing tells us that the poison has interfered with the body's ability to turn off the stimulation of the muscle cell. Organophosphate poisons inhibit the activity of acetylcholinesterase. Acetylcholinesterase breaks down acetylcholine at the neuromuscular junction and limits the length of time the acetylcholine stimulates the postsynaptic terminal of the muscle fiber. Under organophosphate poison

influence, acetylcholine accumulates in the synaptic cleft and continuously stimulates the muscle fiber. As a result, the muscle remains contracted until it fatigues. Death is caused by the victim's inability to breathe. Either the respiratory muscles are in spastic paralysis or they are so depleted of ATP that they cannot contract at all.

Chapter 8

1. Recall that action propagation occurs more rapidly along myelinated axons. If one series of neurons were unmyelinated and the other myelinated, the unmyelinated series would be slower. Also, the question does not say the series are the same size. If one series of neurons had more neurons, it would have more synapses, which would slow down the rate of action propagation.

3. a. To answer this question we need to identify the nerve associated with the upper limb, particularly associated with its extension. In table 8.3 we see that the radial nerve innervates the posterior (extensor) muscles of the arm and forearm. When these muscles are paralyzed, the flexor muscles are unopposed and result in the flexed limb described.

   b. Similar to answer part a, we need to identify the nerve involved in the extension of the lower limb. From table 8.3 we see that the femoral nerve innervates the extensor muscles of lower limb.

5. The blow to the head erased Landon's short-term memory, which would have extended to about 10 minutes before the blow. Because that information was never transferred to long-term memory Landon is unable to recall the events just prior to his accident.

7. Recall that the nervous system stimulation of the digestive system is mainly controlled by the parasympathetic division, and occurs primarily through the vagus nerve (cranial nerve X), which arises from the brain. Therefore, an injury to the spinal cord at the level of C6 does not affect the functioning of this nerve.

Chapter 9

1. By reviewing figure 9.14, we can see that the lenses of the eye are biconvex structures. The lenses are most important in close vision as they are thickened (made more convex) by relaxation of the suspensory ligaments (accommodation). Therefore, if they were removed, close vision would be most affected, and convex glasses would do the best job of replacing the lenses for near vision, such as when reading.

3. We learned that under normal conditions, pressure changes in the middle ear occur through the auditory tube. The auditory tube connects the middle ear to the pharynx, which opens to the outside of the body through the oral and nasal cavities. This allows air pressure to equalize on both sides of the tympanic membrane. When a person is under water, the increased water pressure on the outside of the tympanic membrane forces it toward the middle ear because the external water pressure exceeds the air pressure in the middle ear. As a result, the tympanic membrane cannot vibrate as freely as when the pressure is equalized. Vibration of the tympanic membrane is an important part of sound transmission to the inner ear. The lack of vibration of the tympanic membrane results in a decrease in hearing. If the pressure difference becomes too great, it can rupture the tympanic membrane.

5. To answer this question, review the lacrimal apparatus illustrated in figure 9.7*c*. When a contaminated hand rubs the eyes, the virus can be introduced into tears on the conjunctiva. From there the virus can spread into the lacrimal canaliculi and pass through the nasolacrimal duct into the nasal cavity.

Chapter 10

1. The question tells us that a particular hormone works through a membrane-bound receptor. Because inhibition of cAMP destruction increases the response to the hormone, we can conclude that activation of the receptor induces cAMP production. In addition, the question tells us that inhibition of GTP binding reverses the increased response. We can further conclude that the cAMP production is dependent on a G protein mechanism.

3. Vitamin D increases the rate of transport of Ca^{2+} across the wall of the intestine. Therefore, in response to high concentrations of vitamin D, blood Ca^{2+} levels can become abnormally high. Because the blood Ca^{2+} levels are elevated, the rate of PTH secretion decreases to low levels. Also, the elevated blood Ca^{2+} levels stimulate calcitonin secretion.

5. Aldosterone stimulates increased Na^{+} reabsorption from urine into the blood. Due to osmosis of water toward a higher solute concentration in the blood, urine volume decreases. Water movement into the blood increases blood volume and thus blood pressure. Aldosterone also stimulates removal of K^{+} from the blood. The K^{+} is secreted into the urine. Thus, increased aldosterone promotes higher blood pressure and low blood K^{+} levels.

7. Stressful conditions cause increased ACTH secretion. Increased ACTH stimulates the secretion of glucocorticoids, such as cortisol. One of the effects of increased cortisol secretion is inhibition of the immune response. This could lead to an increased likelihood of a variety of infections, including colds and other diseases. Stomach pains may be due to inflammation of the stomach. Many stomach ulcers result from inflammation caused by bacteria.

Chapter 11

1. Blood doping increases the number of red blood cells in the blood. In this chapter we learned that the major function of red blood cells is to carry oxygen to the tissues of the body. By increasing the number of red blood cells, blood doping increases oxygen delivery to the tissues, such as skeletal muscle. Oxygen is used by these cells to produce ATP, the energy needed for normal cell activity. As a consequence, we would expect that Jackson would not tire as easily during the race. However, the increased number of red blood cells also makes it more difficult for the blood to flow through the blood vessels, increasing the workload on the heart. The same effect is seen in erythrocytosis (polycythemia). In addition, if the process is not done properly, there is a risk of infection.

3. The hypoventilation results in decreased blood O_2. In this chapter we learned that this would stimulate the release of erythropoietin from the kidneys. The erythropoietin stimulates red blood cell production in the red bone marrow. Consequently, red blood cell numbers increase.

5. Vitamin B_{12} and folate are necessary for blood cell division. Lack of these vitamins results in anemia. Iron is necessary for the production of hemoglobin. Lack of iron results in iron-deficiency anemia. Vitamin K is necessary for the production of many blood-clotting factors. Lack of vitamin K can greatly increase blood-clotting time.

Chapter 12

1. In this chapter we learned that a heart murmur is an abnormal heart sound. We also learned that an ECG monitors the electrical activity of the heart, not heart sounds. So, it is unlikely that an ECG would be used to reveal a heart murmur. Instead, a stethoscope is a more likely instrument for detecting a heart murmur. A condition that causes a heart murmur could also cause an obvious abnormality in the ECG, but that is not always the case.

3. Cutting sensory nerve fibers from baroreceptors would reduce the frequency of action potentials delivered to the medulla oblongata from the baroreceptors. This results because the normal blood pressure stimulates the baroreceptors. By reviewing figure 12.21, we see that an increase in blood pressure increases the action potential frequency, and a decrease in blood pressure decreases the action potential frequency. Because cutting the sensory nerve fibers decreases the action potential frequency, this acts as a signal to the medulla oblongata that a decrease in blood pressure has occurred, even though the blood pressure has not decreased. The medulla oblongata responds by increasing sympathetic action potentials and reducing parasympathetic action potentials delivered to the heart. Consequently, the heart rate increases.

5. Recall that Ca^{2+} is involved in the depolarization of the cardiac muscle cells. If less Ca^{2+} flows into the cardiac muscle cells, the rate and degree of depolarization decrease. The result is that action potentials develop more slowly and depolarization does not occur to the normal degree. Slower development of action potentials slows the heart rate. The degree of depolarization causes less Ca^{2+} to enter the cell; consequently, the force of contraction decreases. Therefore, a drug that blocks Ca^{2+} channels decreases the heart rate and the force of heart contraction.

7. Recall that cardiac output is influenced by the heart rate and stroke volume ($CO = SV \times HR$). An athlete's cardiac output can be equal to a nonathlete's cardiac output while they are both at rest, even though the athlete's heart rate is lower than the nonathlete's heart rate,

because the stroke volume of the athlete's heart is greater than the stroke volume of the nonathlete's heart. Athletic training causes a gradual hypertrophy (enlargement) of the heart. Therefore, an athlete can maintain a cardiac output that is equal to a nonathlete's because the athlete has an increased stroke volume but a decreased heart rate. During exercise, an athlete's heart rate and stroke volume increase. The stroke volume of the athlete's heart is much greater than the stroke volume of the nonathlete's. Therefore, the cardiac output of the athlete's heart is greater than the cardiac output of the nonathlete's during exercise.

9. An incompetent aortic semilunar valve is leaky. Thus, when it is closed, blood is able to leak through it back into the left ventricle from the aorta. The aortic semilunar valve is normally closed from the beginning of ventricular diastole until just after the beginning of ventricular systole. During ventricular diastole, blood flows from the left atrium into the left ventricle. If the aortic semilunar valve is leaky, blood will also flow through the aortic semilunar valve into the left ventricle. Consequently, the volume of the left ventricle and the pressure in the left ventricle become greater than normal during ventricular diastole. Because blood is leaking from the aorta, the aortic pressure, during ventricular diastole, is lower than normal in the aorta. Because of Starling's law of the heart during ventricular systole, the ventricular muscle contracts with a greater force and forces a greater volume of blood into the aorta. Consequently, the pressure in the left ventricle is greater than normal during ventricular systole. Also, pressure in the aorta is greater than normal during ventricular systole.

Chapter 13

1. a. Figure 13.5 will be very helpful when answering this question. We can see from the diagram that as a red blood cell leaves the left ventricle and moves to the right side of the brain, it will pass through the following: the aorta, the brachiocephalic artery, and the right common carotid artery, the right internal carotid artery, and the cerebral arterial circle. For the left side of the brain: the red blood cell would pass through the aorta, the left common carotid artery, and the left internal carotid artery, and the cerebral arterial circle.

   b. Figures 13.5 and 13.7 will also be helpful as we describe the pathway for this question. We can see from the diagram that a red blood cell leaves the left ventricle and moves to the left external portion of the skull: the aorta, the brachiocephalic artery, and the right common carotid artery, and the right external carotid artery. For the left side of the external portion of the skull: a red blood cell would pass through the aorta, the left common carotid artery, and the left external carotid artery.

   c. Figure 13.5 will be useful when answering this question. We can see that a red blood cell leaving the left ventricle would pass through the following vessels as it moves toward the left hand: the aorta, the left subclavian artery, the left axillary artery, the left brachial artery, and either the left radial or the ulnar artery.

   d. Figure 13.5 will be useful when answering this question. We can see that a red blood cell leaving the left ventricle would pass through the following vessels as it moves toward the anterior portion of the right leg: the aorta, the right common iliac artery, the external iliac artery, the femoral artery, the popliteal artery, and the anterior tibial artery.

3. The femoral artery and vein are close to the surface in the femoral triangle, which is in the superior and medial part of the thigh. The femoral artery is the vessel into which the catheter will be placed. The femoral vein cannot be used because extending a catheter

superiorly in the femoral vein will deliver the catheter to the right side of the heart. The anterior interventricular artery is a branch of the left coronary artery, which originates from the ascending aorta, just superior to the aortic semilunar valve. The catheter is inserted into the femoral artery. Using figure 13.5, we can trace the path to the heart. From the femoral artery, the catheter passes through the external iliac artery, through the common iliac artery, and through the aorta. It passes through the abdominal aorta, the thoracic aorta, and the aortic arch to the beginning of the left coronary artery and then to the anterior interventricular artery.

5. Recall that atherosclerosis is a form of arteriosclerosis caused by the formation of plaques in blood vessel walls. This narrows the passageway through the blood vessel, thereby reducing blood flow. Reduced blood flow to the kidney stimulates renin secretion. Renin acts on angiotensinogen to produce angiotensin I. Angiotensin I is converted to angiotensin II by the action of angiotensin-converting enzyme. Angiotensin II causes vasoconstriction, which increases blood pressure. In addition, angiotensin II stimulates the secretion of aldosterone from the adrenal cortex. Aldosterone acts on the kidney, causing the reabsorption of Na^+ and water, thus increasing the blood volume. The increased blood volume results in increased blood pressure.

7. Dilation of arteries and veins allows blood to accumulate in the dilated blood vessels. Consequently, less blood is returned to the heart (decreased venous return). Because the venous return is reduced, the stroke volume of the heart decreases (see Starling's law of the heart—chapter 12). Consequently, the heart does less work and less O_2 is required to support the contraction of the heart. Therefore, angina pains, which are caused by inadequate O_2 delivery to the heart muscle, are reduced.

Chapter 14

1. One function of the lymphatic system is to return excess fluid from the tissues to the circulation. Elevation of the limb allows gravity to assist the movement of lymph toward the heart. Massage moves lymph through the lymphatic vessels in the same fashion as does contraction of skeletal muscle. The application of pressure periodically to lymphatic vessels forces lymph to flow toward the trunk of the body, but valves prevent the flow of lymph in the reverse direction. The removal of lymph from the tissue helps relieve edema.

3. Recall that antigens stimulate immune response. Also, remember that due to active acquired immunity, secondary responses to antigens produce greater amounts of antibodies.

5. If the patient has already been vaccinated, the booster shot stimulates a memory (secondary) response and rapid production of antibodies against the toxin. If the patient has never been vaccinated, vaccinating him is not effective because there is not enough time for the patient to develop his own primary response. Therefore, an antiserum is given to provide immediate, but temporary, protection. Sometimes both are given: The antiserum provides short-term protection and the tetanus vaccine stimulates the patient's immune system to provide long-term protection. If the shots are given at the same location in the body, the antiserum (antibodies against the tetanus toxin) could cancel the effects of the tetanus vaccine (tetanus toxin altered to be nonharmful).

7. Samantha experienced two different types of tissue damage resulting in inflammation. Poison ivy caused an allergic reaction resulting in excessive inflammation. The ointment, which reduces inflammation, was ideal for treating this condition. When she scraped her elbow, she became prone to bacterial infection. In this situation, inflammation is a positive immune response to help protect from infection. Applying the ointment would not be a good idea in this case.

Chapter 15

1. The back pressure/arm lift method causes ventilation of the lungs because the process changes thoracic cavity volume to mimic breathing. Pressing firmly on the bases of the scapulae depresses the thoracic cavity, reducing its volume. The reduced volume increases alveolar pressure enough to allow air to leave the lungs (exhale). Next, lifting the arms allows gravity to cause the enlargement of the thoracic cavity. The larger volume in the thoracic cavity reduces alveolar pressure and air flows into the lungs (inhale).

3. The most likely difference would be that her vital capacity would be greatest when she is standing up. In the upright position, gravity tends to pull the abdominal organs downward. As a result, movement of the diaphragm is not as restricted and thoracic volume is increased. Lying down allows abdominal organs to exert pressure on the diaphragm, decreasing the thoracic volume.

5. As fluid accumulates in the alveoli, the layer through which O_2 and CO_2 must diffuse in the alveoli becomes thicker. As the layer thickens, the rate at which gases diffuse slows. Consequently, the amount of O_2 that diffuses into the pulmonary capillaries is reduced and the amount of CO_2 that diffuses out of the pulmonary capillaries decreases. The decreased blood O_2 levels and the increased CO_2 levels stimulate the respiratory center and cause the rate and depth of respiration to increase. Oxygen therapy increases the Po_2 in the alveoli and reduces the Pco_2 in the alveoli. Therefore, O_2 diffuses more rapidly from the alveoli into the pulmonary capillaries and CO_2 diffuses more rapidly from the pulmonary capillaries into the alveoli. This establishes more normal blood levels of O_2 and CO_2. Because of increased levels of O_2 and decreased levels of CO_2 in the blood, the rate of respiratory movements is decreased.

7. The pH of the body fluids in patients who suffer from untreated diabetes mellitus decreases (becomes more acidic). A decreasing pH acts as a strong stimulus to the respiratory center. Consequently, the

rate and depth of respiration increase. The increased rate and depth of respiration cause CO_2 to be released from the circulation at a greater rate. The lower blood level of CO_2 opposes the reduced pH because of the following reaction:

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

As more CO_2 is removed from the blood, more H^+ and HCO_3^- combine to form H_2CO_3. Removal of the H^+ from the circulation resists a further reduction in the body fluid pH.

9. Hyperventilating before swimming decreases the amount of CO_2 in the blood. The decreased amount of CO_2 allows a longer than normal period of time before the swimmer has a strong urge to breathe. This can be dangerous, however, because the reduced level of CO_2 causes vasodilation in the periphery and reduced blood flow to the brain and could cause a person to pass out. Passing out under water could lead to drowning.

Chapter 16

1. Although the swallowing reflex is lost, the vomiting reflex is intact. Vomit can enter the larynx and trachea, and block the respiratory tract. This would keep the patient from breathing. Acidic stomach secretions cause severe inflammation and swelling of the respiratory passages.

3. Even though bacteria apparently cause most ulcers, overproduction of hydrochloric acid because of stress is a possible contributing factor. Antibiotic therapy is an effective treatment, but reducing hydrochloric acid production is recommended. Possible solutions also include drugs that reduce stomach acid secretion, antacids to neutralize the stomach acid, smaller meals (distention of the stomach stimulates acid production), and proper diet. The person should avoid alcohol, caffeine, and large amounts of protein because they stimulate acid production. She should ingest fatty acids because they inhibit acid production, causing the release of gastric inhibitory polypeptide and cholecystokinin. Stress also stimulates the sympathetic nervous system, which inhibits duodenal gland secretion. As a result, the duodenum has less of a mucous coating and is more susceptible to gastric acid and enzymes. Relaxing after a meal helps decrease sympathetic activities and increase parasympathetic activities.

Chapter 17

1. To answer this question, we must first recall the recommended daily value for saturated fats. The recommended daily consumption of saturated fats is less than 20 g. We can now calculate the percentage of the recommended value this particular food provides by dividing the amount by the recommended daily consumption. Therefore, the % Daily Value for 2 g of fat is 10% (2 / 20 = 0.10, or 10%).

3. From question 2, the teenager's daily maximum amount (weight) of fat consumed per day is 100 g. If he consumes a 10-g serving of fat, his % Daily Value is 10% (10 / 100 = 0.10, or 10%).

5. An active person uses many more kilocalories in a day than a person who is not active, and so can lose weight on a higher-kilocalorie diet. In addition, some people have a higher basal metabolic rate and tend to burn more kilocalories.

7. Sandra's urine would have more urea than before she began the high-protein diet. Excess protein is metabolized and used as a source of energy. One of the breakdown products of protein is ammonia. Ammonia is toxic, so it is converted in the liver to urea, which is carried by the blood to the kidneys and eliminated.

9. No, this approach does not work because he is not losing stored energy from adipose tissue. In the sauna, he gains heat, primarily by convection from the hot air and by radiation from the hot walls. The evaporating sweat is removing heat gained from the sauna. The loss of water will make him thirsty, and he will regain the lost weight from drinking fluids and eating foods containing water.

11. During fever production, the body produces heat by shivering. The body also conserves heat by constricting blood vessels in the skin (producing pale skin) and by reducing sweat loss (producing dry skin). When the fever breaks—that is, "the crisis is over"—heat is lost from the body to lower body temperature to normal. This is accomplished by dilation of blood vessels in the skin (producing flushed skin) and increased sweat loss (producing wet skin).

Chapter 18

1. Because Thiago consumed a large volume of hyposmotic (dilute) fluid in a short period of time, the first consideration is the effect on blood volume. Drinking this much dilute fluid increased Thiago's blood volume and decreased the solute concentration of his blood. The increased blood volume is detected by baroreceptors, and the decreased solute concentration is detected by specialized neurons in the hypothalamus. The response to the low blood solute concentration is inhibition of ADH secretion. The increased blood volume inhibits the renin-angiotensin-aldosterone mechanism, which in turn inhibits aldosterone secretion. As a result of these changes, the rate of urine production increased over the next 2 hours and the urine was dilute. Once blood volume and solute concentration return to normal, the rate of urine production will slow back to normal.

3. Excessive sweating results in a loss of water and solutes. However, the degree of water loss is more significant than the degree of solute loss, which decreases blood volume. The decreased blood volume increases the solute concentration of the blood. Both of these changes stimulate ADH secretion, which results in production of a small volume of concentrated urine.

5. The following all decrease the blood pressure in the glomerular capillaries and therefore decrease the glomerular filtration rate: decreased blood pressure and increased sympathetic stimulation that constricts the renal arteries and the afferent arterioles. Blocking the nephron causes the capsule pressure in the nephron to increase, so that it is equal to the pressure in the glomerular capillaries, which reduces the filtration rate. An increase in plasma proteins also decreases the filtration rate. The increased plasma protein concentration attracts water by osmosis and therefore reduces the tendency for water to pass from the glomerulus to Bowman capsule.

7. While Sadiq held his breath, CO_2 accumulated in his body fluids. The increased CO_2 reacted with water to form carbonic acid that, in turn, produced H^+ and HCO_3^-. The increased concentration of H^+ in the body fluids caused the pH of the body fluids to decrease. After 2

minutes, the reduced pH and increased body fluid CO_2 levels strongly stimulated the respiratory center to increase the rate and depth of respiration. The increased rate of respiration reduced the body fluid CO_2 levels and increased the body fluid pH back toward its normal value. The kidneys did not respond to the change in pH within 2 minutes. The kidneys are more powerful regulators of body fluid pH, but they require several hours to become maximally active.

Chapter 19

1. Removing the testes eliminates the source of testosterone. Therefore, blood levels of testosterone would decrease. Because testosterone has a negative-feedback effect on the hypothalamus and pituitary gland, GnRH, FSH, and LH secretion increases and the blood levels of these hormones increase.

3. The secretory phase of the menstrual cycle occurs after ovulation. It is following ovulation that the corpus luteum forms and produces progesterone. In addition, the progesterone acts on the endometrium of the uterus to cause its maximum development. Therefore, progesterone secretion reaches its maximum levels and the endometrium reaches its greatest degree of development during the secretory phase of the menstrual cycle.

5. On day 15 of the menstrual cycle, one would expect decreasing blood levels of LH, decreasing blood levels of estrogen, and increasing blood levels of progesterone. In the average menstrual cycle, ovulation occurs on day 14. After ovulation, the ovulated follicle develops into the corpus luteum. Estrogen levels decrease as the follicle is converted to the corpus luteum. The corpus luteum secretes progesterone in increasing quantities and small amounts of estrogen as the corpus luteum develops. The increasing blood levels of progesterone inhibit LH secretion from the pituitary gland. Consequently, blood levels of LH fall to low levels.

7. During menopause, estrogen and progesterone are produced by the ovary in only small amounts. Consequently, estrogen and progesterone levels in the blood are low. These hormones have a negative-feedback effect on the secretion of FSH and LH from the anterior pituitary gland. Therefore, in the absence of estrogen and progesterone, FSH and LH are secreted in greater amounts and the blood levels of FSH and LH increase. However, there is no large increase in LH, like the increases that occur prior to ovulation. The average concentration of LH and FSH is greater than the levels that occur either before or after ovulation.

Chapter 20

1. Recall that fertilization occurs approximately 14 days after the LMP, so the embryo in this case is 30 days old. We can see from table 20.2 that the fetus has just completed the “budding” period; limb buds and other “buds” have just formed.
3. The correct answer is A. Recall that prolactin is responsible for the production of milk by the breast. Surges of prolactin are stimulated by the process of suckling and are required to maintain milk production. Drugs that inhibit prolactin release will cause the breast to cease milk production after a few days.
5. No, not without additional information. To be able to roll their tongue into a tube, both mother and son need to have only one dominant gene. The son could inherit this dominant gene from his mother, so it is possible that his father is a non-tongue roller. It is also possible that his father is a tongue roller, but there is no proof for either hypothesis.

Appendix E

Answers to Odd-Numbered Apply It Questions

Chapter 1

Learn to Apply It

The Learn to Apply It feature in every chapter of this text is designed to help you develop the skills to successfully answer critical thinking questions. The first step in the process is always to analyze the question itself. In this case, the question asks you to evaluate the mechanisms governing Renzo's blood sugar levels, and it provides the clue that there's a homeostatic mechanism involved. In addition, the question describes a series of events that helps create an explanation: Renzo doesn't feel satisfied after eating, has elevated blood sugar, and then is prescribed an insulin pump. In chapter 1, we learn that homeostasis is the maintenance of a relatively constant internal environment. Renzo experienced hunger despite eating, and his blood sugar levels were higher than normal. In this situation, we see a disruption in homeostasis because his blood sugar stayed too high after eating. Normally an increased blood sugar after a meal would return to the normal range due to the activity of insulin secreted by the pancreas. When blood sugar returns to normal, insulin secretion stops. In Renzo's case, his pancreas has stopped making insulin. Thus, the doctor prescribed an insulin pump to take over for his pancreas. Now when Renzo eats, the insulin pump puts insulin into his blood and his blood sugar levels are maintained near the set point.

1. To answer this question, you must first realize that regulation of our body's environment is due to homeostatic mechanisms. These mechanisms work to keep variables near their set point. In this chapter, you learned that in order to keep body temperature near its set point, the control center (the hypothalamus), receives input from thermoreceptors in the skin. The hypothalamus would then instruct the effectors (the sweat glands) to produce sweat if body temperature had risen too high. So, for this question, you can predict that swimming in cool water would prevent the hypothalamus from stimulating the sweat glands to produce sweat. The next part of the question asks what would happen if this mechanism was not sufficient to maintain normal body temperature. In other words, if you were swimming in cool water, the thermoreceptors would cause the hypothalamus to initiate shivering. Simply preventing sweating was insufficient to keep body temperature from dropping out of its normal range. If shivering continued to be ineffective, the body would conserve heat through loss of consciousness and severe hypothermia could set in.

3. In order to recognize which correct term to use here, you must first realize that directional terms are relative terms to the body. Therefore, it doesn't matter what position your body is in compared to the earth, body parts always have the same relationship to each other. Thus the nose is always referred to as being superior to the mouth.
5. The first step is to define the abdominopelvic and peritoneal cavities. The abdominopelvic cavity is located inferiorly to the diaphragm and superiorly to the pubic symphysis. The peritoneal cavity is located between the visceral peritoneum, which covers organs in the abdominopelvic cavity, and the parietal peritoneum, which lines the wall of the abdominopelvic cavity. So, look at figure 1.13*c* and take notice of the bright white area. This is the peritoneal cavity containing only peritoneal fluid. You can see that, although the peritoneal cavity is around these organs, they are not within the peritoneal cavity. Secondly, looking at the right side of figure 1.13*c* again, notice there are organs behind the parietal peritoneum, but inside the abdominopelvic cavity. These organs are also not within the peritoneal cavity and are considered retroperitoneal (e.g., the kidneys).

Chapter 2

Learn to Apply It

In this question, you learn that Rafael had not been able to properly hydrate the night before the soccer match and the weather is hot. The question also tells you that Rafael was cool when he was sweating and became overheated when he stopped sweating. Sweat consists mainly of water, and as you learned in section 2.1, water molecules are polar, allowing them to hydrogen-bond together. Later, in section 2.4, you learned that hydrogen bonds stabilize water, allowing it to absorb large amounts of heat. Thus, sweating effectively creates a cooler layer of air next to your skin because the water molecules in sweat can absorb heat. Because Rafael was dehydrated, he could not continue sweating, became overheated, and suffered mild heat stroke.

1. The question asks you to differentiate between mass and weight. First, consider the definitions. Weight, in particular, is dependent on the force of gravity. Therefore, if an astronaut is in outer space, where the force of gravity from earth is nearly nonexistent, the astronaut is "weightless." However, the definition of mass is the amount of matter present in the object itself. Thus, no matter the location of an object, the mass remains constant.
3. A fun, easy way to remember how loss of electrons affects the charge of an atom is to ask: "Atom, are you sure you lost an electron?" Atom: "I'm positive." Therefore, we know that the charge on an iron ion would be positive. The charge is also equal to the number of electrons lost, in this case, 3. Therefore, the iron's charge would be +3 and the symbol is Fe^{3+}.
5. During exercise, your body is doing work by muscular contractions. Work involves converting one form of energy into another, and as you read in the previous section, this conversion is not 100% efficient. As a result, heat energy is released. When you contract your muscles, potential energy is converted to kinetic energy and heat energy. Thus, more heat is produced than when at rest, and your body temperature increases.

Chapter 3

Learn to Apply It

Consider the important points made in the question. First, Carlos suffers from a genetic disease (diabetes insipidus), and second, this disease results in excessive water loss at the kidneys. In this chapter we learned that DNA contains the information for directing protein synthesis. Because diabetes insipidus is a genetic disease, one possible conclusion is that some type of protein is not functioning correctly. We also learned that proteins have several functions, including acting as receptor molecules and membrane channels. Malfunction of either of these type of proteins could disrupt water homeostasis. ADH is a chemical signal that regulates water loss at the kidneys. If the receptor molecules for ADH are altered and not functioning properly, the kidney cells would not respond to the signal. Another possibility is that water membrane channels, which allow water to move across the cell membrane, are not functioning properly and are disrupting water homeostasis.

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1. First, we need to consider the normal process and identify the intracellular and extracellular areas involved. We are told that urea diffuses from liver cells, which is the intracellular region, to the blood, which is the extracellular region. This also defines the direction of urea diffusion, from the area of higher urea concentration inside the cells to the area of lower urea concentration in the blood. The kidneys remove the urea from the blood; therefore, if the kidneys stopped functioning, the concentration of urea in the blood would increase. Eventually, this would eliminate the urea concentration gradient or even reverse it. Urea would remain in the cells and increase to toxic levels that could damage or even kill the cells.
3. In the description of cystic fibrosis we learn that it is the result of defective chloride ion channels that fail to transport Cl^- out of cells. This description allows us to easily predict the effect on Cl^- concentrations inside and outside of the cell, because ion channels allow ions to diffuse down their concentration gradients. The concentration of Cl^- would remain higher inside the cell and lower outside the cell.
5. Recall from “Gene Expression” that a gene is a sequence of DNA nucleotides that provides the instructions for making a specific protein. We also learned

that the sequence of DNA nucleotides determines the sequence of RNA nucleotides of an mRNA, which then determines the sequence of amino acids of a protein in the processes of transcription and translation, respectively. We also learned that the information in mRNA is carried in three nucleotide groups called codons, which specify a particular amino acid or signal the end of translation. So, if one nucleotide in a DNA molecule is changed, that one codon in the mRNA molecule will also be changed. This can lead to several different outcomes. Since an amino acid can often be specified by more than one codon, the changed nucleotide may not change the amino acid and hence the protein structure will not be affected. Alternatively, the changed nucleotide may change the codon to specify a different amino acid. This single amino acid change could in turn change the protein structure. Depending on the changed amino acid, the structural change could be subtle or severe. Finally, the changed nucleotide could create a new stop codon or eliminate an existing stop codon. These changes would very likely cause dramatic changes in the protein structure since a premature stop codon would cut the protein short and removal of a stop codon would add extra amino acids not normally in the protein.

Chapter 4

Learn to Apply It

The question tells us that gluten enteropathy affects the intestinal lining, reducing its ability to absorb nutrients and water. It also reminds us that the absorption of nutrients and water occurs at the cellular level via several different transport processes. Let's first identify the tissue type affected by gluten enteropathy. In this chapter we learned that epithelial tissue covers body surfaces, including the lining of the intestines. Further reading showed that the intestinal lining is composed of simple columnar epithelial tissue. Therefore, the tissue type affected by Matt's gluten enteropathy is simple columnar epithelium. We are then asked to identify the specific cell parts affected by this disease. As stated in the question, the intestinal lining is organized into fingerlike projections called villi, which are covered by the simple columnar epithelium. We also learned that the epithelial cells of this tissue have microvilli. In chapter 3 we learned that microvilli are extensions of the plasma membrane that increase the surface area for absorption. Matt's gluten enteropathy reduced his ability to absorb nutrients and water, so we can conclude that the cell parts affected by the disease are the microvilli. Finally, the question asks us to explain why Matt suffers from bouts of diarrhea after eating gluten. We know that gluten damages the intestinal lining by decreasing the number of villi and microvilli. This reduces the surface area for absorption. If the surface area decreases, fewer nutrients are absorbed. Chapter 3 showed us that water moves by osmosis to areas of higher solute concentration. The nutrient molecules are solutes in the intestines. Because the solutes are not being absorbed, the solute concentration remains high in the intestines, and water absorption decreases. As a result, the nutrients and water accumulate in the intestines, resulting in the watery feces of diarrhea.

1. a. The question asks about the relationship between form and function of tissues. First, consider the name of the tissue type: nonkeratinized stratified epithelium. The term stratified means more than one layer of cells, whereas, the term simple means a single layer of cells. In the digestive tract, a principal function is absorption, a process that would be hindered by the many layers of stratified epithelium. Stratified epithelium is more suited to areas where the layers would protect underlying tissues from abrasion. Columnar cells are specialized for secretion and absorption.

These cells contain a large number of organelles that produce the secretions and transporters needed to support absorption.

b. In this scenario, both tissue types are stratified, but one type lacks keratin. The protein keratin provides a tough layer that retards water movement. If keratin were absent from the epidermis, the body could not retain water effectively and would be more prone to damage from abrasion.

3. The question tells you that: (1) vitamin C is required for collagen formation; (2) scars are formed from collagen; and (3) there is a lack of vitamin C. Therefore, if there is a lack of vitamin C, the density of collagen fibers in a scar may be reduced and the scar may not be as durable as a normal scar.

5. There is more than one way to organize a table that summarizes the characteristics of the major muscle types. See table E. I.

7. The question asks why stitches are helpful for healing a wound with a large space between the edges. Sutures bring the edges of a wound closer together so that there is (1) less space for regenerating cells to fill in; (2) a lower risk of infection; (3) a reduced amount of granulation tissue formation; and (4) a faster healing time. Additionally, the smaller amount of scar tissue and wound contracture lessens the visibility of the wound site later on.

Chapter 5

Learn to Apply It

In the section "Skin Color," we learned that melanocytes located in the epidermis produce melanin, a group of pigments that provide protection against ultraviolet light from the sun. We also know that the amount of melanin produced is determined by several natural factors, including our genes. We can assume that Mia and Landon naturally have darker skin than Christine, because they each possess genes that allow them to produce more melanin when exposed to ultraviolet light. Recall also from the Clinical Impact feature "Skin Cancer" that we can artificially block ultraviolet light by applying sunscreens. Christine's mother may have forgotten to apply sunscreen on Christine during the day or used a sunscreen that didn't effectively block UVB, which commonly causes sunburn.

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Table E.1 Major Characteristics of the Three Muscle Types

Muscle Type	Nuclei in Each Cell	Location of Nuclei	Control	Cell Shape	Striated	Branching Fibers
Skeletal	Many	Peripheral	Voluntary	Long and cylindrical	Yes	No
Cardiac	One	Central	Involuntary	Branching cylinders joined by intercalated disks	Yes	Yes
Smooth	One	Central	Involuntary	Spindle-shaped cells	No	No

1. In the description of the epidermis, the superficial layer of the skin, we learned that the keratinized cells are coated with lipids to prevent fluid loss. Recall from chapter 3 that substances that are lipid-soluble easily diffuse through lipid layers but water-soluble substances do not. By applying the same principles of diffusion across cell membranes to diffusion across the skin, we can predict that lipid-soluble substances diffuse easily but water-soluble substances do not.

3. Recall that hair color is determined by the production and distribution of melanin by melanocytes in the hair bulb. Also, remember that hair growth begins at the hair bulb and that the pigmented cells are pushed farther and farther away from the hair bulb, as the hair grows longer. This would make it impossible for Marie Antoinette's hair to suddenly turn white; only new hair growth would show the loss of pigment. Since it takes quite a while for hair to grow, it is impossible that her hair could turn white in one day.

5. We learned that one of the functions of the skin is to reduce water loss. Sam's burns resulted in severe damage to his skin, which most likely led to increased water loss at the injury site, causing dehydration and reduced urine production. We learned that Sam was administered a large volume of fluid to counteract his increased fluid loss. But how much fluid should be given? The amount of fluid given should match the amount that is lost, plus enough to keep the kidneys functioning properly. An adult receiving intravenous fluids should produce 30-50 mL of urine per hour, and children should produce 1 mL/kg of body weight per hour. By monitoring Sam's urine output, the nurse can determine if he is getting enough fluids. If his urine output is too low, more fluids can be given.

Chapter 6

Learn to Apply It

Because the question tells us that Dr. Miller suffers pain when he bends over, it is most likely that he has a ruptured intervertebral disk in his lumbar region. When these disks rupture, a portion of the disk protrudes and pushes against the spinal cord or the spinal nerves, compromises their function, and produces pain. Herniation of the inferior lumbar disks is most common because, as you learned in section 6.10, the lumbar vertebrae support more weight than other regions of the vertebral column. Dr. Miller's ruptured disk might be repaired with prolonged bed rest or it might require surgery. One such type of surgery involves removing the ruptured disk and replacing it with a piece of hipbone. Eventually the adjacent vertebrae will become fused by bone across the gap.

1. In the previous section, you learned that the minerals of bone give it weight-bearing strength much as concrete provides strength to columns of a bridge. Without the minerals, the bone matrix would consist of only collagen and would be overly flexible—it could be tied into a knot. On the other hand, you learned that collagen springs back to its original shape after it has been bent. Therefore, without collagen, bone would be too brittle and would easily break. Collagen loss is one reason the bones of many older people break easily.
3. Because the presence of the osteomyelitis-causing bacteria throws the RANK, RANKL, and OPG system into disarray, any osteoporosis medication that inhibits osteoclast formation could potentially slow the rate of bone loss. In addition, since osteoblasts increase inflammation in the site of infection, anti-inflammatory medication would perhaps slow bone loss that is due to excessive immune system function. However, there is still much work to be done to develop reliable treatments for bone loss prevention during osteomyelitis.
5. Just before the swimmer begins the power stroke, the arm is flexed (close to the body) and medially rotated (towards the center of the body) and the forearm is extended (away from the body) and pronated (palm down). During the power stroke, the arm is powerfully extended (pushed away from the body), slightly abducted (moved away from center), and medially rotated (towards the center of the body). During the recovery stroke, the arm is circumducted (circled around the shoulder towards the back), laterally

rotated (moved away from the center of the body), and flexed (brought closer to the body) in preparation for the next stroke. The forearm is flexed (close to the body) during the first part of the recovery stroke and extended (away from the body) during the last part.

Chapter 7

Learn to Apply It

(a) The first piece of information you are given is that Anthony increased the number of times he was contracting the same muscle group. Looking at figures 7.9 and 7.10, you see that for each cross-bridge formation event, a molecule of ATP is required. Therefore, being able to lift a particular weight once is different from being able to lift that weight many times in a row. Increasing the reps increases the amount of required ATP. You also learned in the section "Fatigue" that depletion of ATP along with decreased pH in muscle cells reduces muscles' work capacity. Lifting the weight rapidly without resting would eventually lead to anaerobic ATP production. This is the reason athletes, in order to build muscle endurance, reduce the weight but increase the number of reps. (b) Looking at figure 7.9, you see that when a muscle contraction is stimulated, Ca^{2+} is released from the sarcoplasmic reticulum. After Anthony had contracted his muscles many times in a row, the level of Ca^{2+} inside his cells was higher than before he started exercising. In addition, the more times a muscle contracts, the more Ca^{2+} is released from the sarcoplasmic reticulum. So, the level of Ca^{2+} in his cells is higher after many reps than when he lifted each weight only once. This is why it is recommended that athletes warm up for at least 15-30 minutes before beginning any strenuous exercise—warming up helps the muscles function as efficiently and powerfully as possible (not to mention that warming up stretches muscles, tendons, and ligaments, which also helps to prevent injury!).

1. To predict a mechanism for anesthetic activity, you must first understand how action potentials are initiated and propagated in electrically excitable cells. In this chapter, you learned that in both nerve cells and muscle fibers, it is Na^+ entry that depolarizes the cell membrane to threshold. Now, recall that at threshold, it is the opening of voltage-gated Na^+ channels that creates the action potential. Thus, you can predict that in order for an anesthetic to prevent action potential formation, it prevents Na^+ channels from opening. Without Na^+ entry, there is no action potential and no transmission of information, such as pain.
3. Referring to figure 7.16 will help you answer this question. Raising eyebrows in surprise—occipitofrontalis; winking—orbicularis oculi; frowning—

depressor anguli oris; sneering—levator labii superioris.

5. In the sprinter's stance and the bicyclist's racing posture, the thigh is flexed at a 45-degree angle because at that angle the gluteus maximus functions at its maximum in extending the thigh, thus providing maximum force.

Chapter 8

Learn to Apply It

The botulism toxins block the release of acetylcholine from neurons. Recall that acetylcholine is a neurotransmitter that is released at neuromuscular junctions, the synapses between neurons and skeletal muscle fibers. Acetylcholine is an excitatory neurotransmitter that stimulates skeletal muscle, causing them to contract. Respiration is dependent on skeletal muscle contraction, particularly by the diaphragm. If acetylcholine release is blocked, Johnny's respiratory muscles will not be stimulated and Johnny will not be able to breathe. Without medical treatment, this could be lethal.

1. To answer this question, let's first describe the Na^+ concentration and its role in a normal excitable cell. We learned that in a normal cell, the concentration of Na^+ is much higher outside the cell than inside the cell. As a result, when Na^+ channels open Na^+ diffuses into the cell quickly causing the changes in the membrane potential that result in an action potential. The movement of Na^+ into the cell is the result of its steep concentration gradient. Remember, also, that enough Na^+ must enter a cell for the membrane potential to reach threshold, opening the voltage-regulated Na^+ channels and causing an action potential. If the extracellular concentration of Na^+ is reduced, then the concentration gradient would also be reduced. The effect would be that if the cell is stimulated, less Na^+ would enter the cell. The cell would not reach threshold and an action potential would not occur.
3. Recall that the phrenic nerve innervates the diaphragm allowing for the contraction necessary for breathing. If the right phrenic nerve was damaged, then we would expect lack of muscle contraction in the right half of the diaphragm affecting breathing. To answer the second part of the question, we need to consider the location of spinal cord injury to predict the effect it would have on the diaphragm. Remember that the phrenic nerve is part of the cervical plexus, which includes spinal nerves C1-C4. If the spinal cord is completely severed in the thoracic region, the phrenic nerve would not be damaged and the diaphragm would not be affected. On the other hand, if the spinal cord is severed in the upper cervical region, the phrenic nerve would be damaged and the contractions of the diaphragm would not occur, eliminating the person's ability to breathe. Death would likely occur if medical assistance was not administered quickly.

5. To answer this question, we need to first identify the type of sensation, the area of the cerebrum that detects this sensation, and the association area that allows for recognition of the object based on past experience. A person that is blindfolded would use the sense of touch to gather information about the object in order to describe it. Sensations from the skin of the hand are sent via sensory neurons to the dorsal horn of the spinal cord. The signals are then relayed to spinal cord neurons and transmitted to the brain. We learned earlier that in the brain, the sense of touch is perceived in the primary somatic sensory cortex of the parietal lobe of the cerebrum and that the somatic sensory association area allows for recognition of the stimulation. The information is passed from the primary somatic sensory cortex to the somatic sensory association area, where she will recognize the characteristics of the object. Now that she has recognized the object, we need to describe the pathway involved in determining a word and initiating the muscle contractions necessary to say the word. This occurs when action potentials travel to the sensory speech area, where the object is given a name. From there, action potentials travel to the motor speech area, where the spoken word is initiated. Action potentials from the motor speech area travel to the premotor cortex and then to the primary motor cortex, where action potentials are initiated that stimulate the muscles necessary to formulate the word.

7. The autonomic nervous system maintains homeostasis by adjusting body activities to different levels of stress and activity. Recall that the sympathetic division of the autonomic nervous system, often called the fight-or-flight system, prepares the body for physical activity but also prepares the body for stressful situations. The parasympathetic division, often called the rest-and-digest system, is consistent with resting conditions. Keeping these descriptions in mind and referring to table 8.8, we can easily answer this question. (a) A person who is extremely angry is experiencing a stressful situation and we would expect changes in the body associated with sympathetic activity to occur. Examples include increased heart rate, increased breathing rate, dilation of pupils, and decreased digestive and urinary function. (b) A person who has just finished eating and is now relaxing would exhibit changes associated with the parasympathetic division. Examples include decreased heart rate, decreased breathing rate, constriction of pupils, and increased digestive and urinary functions.

Chapter 9

Learn to Apply It

The question emphasizes that Freddy is an older man, so we can assume that his vision problems are age-related. In the Effect of Aging box, we learned that presbyopia is the most common age-related change in the eye and results from a decrease in flexibility of the lenses of the eyes. We also learned that we are able to focus images on the retina by changing the shape of the lenses. So, the lenses in Freddy's eyes are less flexible and are less able to focus. But which objects is he having difficulty seeing? He can't focus on objects that are close to his eyes. Recall that the ciliary muscles contract to change the shape of the lenses when viewing close objects. Freddy's joke that his arms are getting shorter just means that he can't hold objects far enough from his face for his eyes to focus on them properly.

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1. To answer the first part of the question, we must recall the types of pain and the types of structures associated with each type of pain. Constipation is causing pain associated with the colon, a deep structure. Remember that the deeper structures lack tactile receptors, so the type of pain experienced is diffuse. We also learned after reading "Referred Pain" that the pain associated with deeper structures is usually felt in more superficial structures. Using figure 9.3, we can predict that the male feels the pain around his navel, the common area for referred pain associated with the colon.
3. After reviewing the section "Lacrimal Apparatus," we understand that tears from the surface of the eyeball drain through the lacrimal canaliculi into the lacrimal sac, which empties into the nasal cavity through the nasolacrimal duct. Our sense of smell is due to the presence of olfactory receptors in the nasal cavity. If medications are placed into the eyes, some may drain into the nasal cavity, which may stimulate the olfactory receptors of the olfactory organ. Our sense of taste is due to the presence of taste receptors in the mouth and pharynx. The ability to "taste" the medication is due to the fluid draining from the nasal cavity into the pharynx stimulating taste receptors.
5. This question addresses changes that occur in the eye as a person looks at things far away and close up. Let's rephrase the question to include whether or not the person is looking at a distant object or a near object. As the person

is driving a car, she is looking at distant objects down the road. She then looks down to see the near speedometer, and then back to the distant objects down the road. Recall that the lenses change shape to focus on objects that are either distant or near. Now consider the changes that occur to the eye, particularly the lens, in the series of events. Referring to figure 9.14 will also help in answering this question. As she is looking at the road (distant), the ciliary muscles of the ciliary body are relaxed, the tension in the suspensory ligaments is high, and the lenses of the eyes are flattened. When she looks at the speedometer (close), the ciliary muscles contract, reducing the tension in the suspensory ligaments, causing the lenses to thicken. When she looks back to the road (distant), the ciliary muscles relax again, increasing the tension in the suspensory ligaments, causing the lenses to flatten again.

7. We learned that the brain compares sensory input from the semicircular canals, eyes, and proprioceptors in the back and lower limbs and that conflicting information can cause motion sickness. If you close your eyes, one of these sources of information is eliminated and the brain has less conflicting input to compare, reducing the probability of motion sickness. We can perceive more motion in close objects than in distant objects, so looking at the horizon would also reduce the visual input of perceived motion to the brain and reduce the probability of motion sickness.

Chapter 10

Learn to Apply It

We learned that Katie has androgen insensitivity syndrome. The name suggests that her tissues are not sensitive to androgens (malelike hormones). We learned that a tissue responds to hormones based on the presence of specific receptors. With androgen insensitivity syndrome, the endocrine malfunction is not in the production of the hormone, such as in insulin-dependent (type 1) diabetes mellitus, but in the receptor in the target cells. Even though her cells produce plenty of the hormone testosterone, the target cells do not respond because the testosterone receptor has malfunctioned and does not recognize testosterone. Katie's feminine appearance is a direct result of the lack of functional testosterone receptors. Katie's body did not develop as a normal male body because her tissues were resistant to testosterone, which is responsible for growth of the male genitalia and other sexual characteristics (see table 10.2 and chapter 19). Therefore, externally Katie looked female when she was born. Without testosterone working in her body or her brain and without normal social cues to associate her with other males, she had always identified herself as female and was devastated to learn she could not have children. Her doctor and mother decided to wait until she was older to explain the entire condition to her.

1. The description of the drug is very important to determining the function of the hormone that it affects. First, the drug is lipid-soluble. Recall that many lipid-soluble hormones bind to intracellular receptors. Next, we learn that the drug prevents the synthesis of messenger RNA. We can therefore predict that the hormone functions by diffusing across the cell membrane and binding to an intracellular receptor. The response of the intracellular receptor is to produce new messenger RNA, which leads to synthesis of new proteins (see chapter 3 for a description of the role of messenger RNA in protein synthesis). The new proteins produce the cell's response to the hormone.
3. Remember that hormones of the hypothalamus and anterior pituitary regulate thyroid hormones. TRH from the hypothalamus stimulates the secretion of TSH from the anterior pituitary. TSH travels to the thyroid to promote secretion of thyroid hormones. In response to the large amount of this protein that is similar to TSH, thyroid hormones are oversecreted by the thyroid gland (hyperthyroidism). Because production of the protein cannot be inhibited by thyroid hormones as TSH is, oversecretion of thyroid gland is

prolonged, and the symptoms associated with hyperthyroidism become obvious. Because TSH stimulates gland growth as well as hormone secretion, the thyroid gland enlarges. In addition, the increased thyroid hormones have a negative-feedback effect on the hypothalamus and pituitary gland. TSH-releasing hormone secretion from the hypothalamus and TSH secretion from the anterior pituitary gland are inhibited.

5. Aldosterone is secreted by the adrenal cortex under low blood pressure conditions and results in increased Na^+ reabsorption and water conservation. Therefore, if aldosterone levels are reduced, less Na^+ is reabsorbed and less water is conserved. This results in a lower blood volume and thus low blood pressure. Aldosterone targets the Na^+-K^+ pump, which if you recall from chapter 3, transports Na^+ and K^+ in opposite directions. So as Na^+ reabsorption decreases due to reduced aldosterone, we would expect elevated blood K^+ levels due to the reduced secretion of K^+. High blood K^+ levels lead to altered nerve and muscle function, which could be life threatening.

7. It's important to understand that a large meal, high in carbohydrates, will increase blood glucose as the nutrients are transported from the small intestine into the blood. The body cells need to take up the glucose across their cell membranes either to utilize it immediately or to store it for later use. Cells take up glucose only in the presence of insulin. Glucose serves as the stimulus for insulin secretion and the inhibitor of glucagon secretion. Thus, after eating, insulin levels increase and glucagon levels decrease. Long before 12 hours has passed after a meal, blood glucose levels drop. Again, it is glucose that serves as the signal for hormone secretion. Now the reduction in blood glucose stimulates glucagon secretion and inhibits insulin secretion. Glucagon then promotes release of stored glucose into the blood to be utilized by cells until the next meal.

9. Removal of part of the thyroid gland reduces the amount of thyroid hormone secreted by the gland. Usually, enough thyroid tissue can be removed to reduce secretion of thyroid hormone to within the normal range. In addition, the remaining thyroid tissue normally does not enlarge enough to produce more thyroid hormone, although there are exceptions. The removal of the thyroid tissue does not remove the influence of the abnormal antibodies on the tissues behind the eyes. Thus, in many cases the condition's effect on the eyes is not improved.

Chapter 11

Learn to Apply It

Jessica's feeling of fatigue and her blood test results are consistent with anemia. A low red blood cell count with microcytic cells, low hemoglobin, and a low hematocrit are all indicators of iron-deficiency anemia. Jessica's low red blood cell count caused less oxygen to be transported to her tissues. Recall that low oxygen levels stimulate the secretion of erythropoietin from the kidneys, which stimulates the production of red blood cells in the red bone marrow. Because of Jessica's iron deficiency, which caused hemoglobin synthesis to slow, the newly synthesized red blood cells were smaller than normal, or microcytic. Remember, Jessica also complained of intense abdominal pain. The evidence of hemoglobin in her feces suggests that Jessica is losing blood from her digestive system, which, given her abdominal pain, would be consistent with having an ulcer. Jessica's doctor would need to order additional tests to confirm the presence of ulcers before determining treatment.

1. To answer this question, we need to first determine the effect carbon monoxide has on red blood cells. Recall from our reading of the function of red blood cells and the description of hemoglobin that carbon monoxide binds very readily to hemoglobin and does not tend to unbind. Therefore, carbon monoxide-bound hemoglobin in red blood cells can no longer transport O_2. This essentially leads to a decrease in blood O_2 levels. We also learned that low blood O_2 levels stimulate red blood cell production by causing the release of erythropoietin, primarily by the kidneys. Erythropoietin stimulates red blood cell production in the red bone marrow. So, we can predict that the number of red blood cells in the person's blood will increase.
3. People with type AB blood were called universal recipients because they could receive types A, B, AB, or O blood with little likelihood of a transfusion reaction. Looking at figure 11.12, you can see that type AB blood does not have antibodies against A or B antigens. Transfusion of these antigens in types A, B, AB, or O blood therefore does not cause a transfusion reaction in a person with type AB blood. The term is misleading, however, for two reasons. First, other blood groups can cause a transfusion reaction. Second, antibodies in the donor's blood can cause a transfusion reaction. For

example, type O blood contains anti-A and anti-B antibodies that can react against the A and B antigens in type AB blood.

5. We learned that HDN is caused by an Rh incompatibility between a pregnant mother with Rh-negative blood and her Rh-positive child. If the mother is sensitized to the Rh antigen, she can produce anti-Rh antibodies that cross the placenta and cause agglutination and hemolysis of fetal red blood cells. To treat HDN with an exchange transfusion, the donor's blood should be Rh-negative, even though the newborn is Rh-positive. Rh-negative red blood cells do not have Rh antigens. Therefore, any anti-Rh antibodies in the newborn's blood do not react with the transfused Rh-negative red blood cells. Eventually, all of the Rh-negative red blood cells die, and only Rh-positive red blood cells are produced by the newborn.

Chapter 12

Learn to Apply It

We learned in this chapter that the heart valves maintain a one-way flow of blood through the heart—from the atria to the ventricles. We also learned that an incompetent valve is one that leaks, or allows some blood to flow in the opposite direction—from the ventricles to the atria. An irregular swooshing noise following the first heart sound, as Stan's regular physician had noticed, is a typical sign of an incompetent valve. The first heart sound is produced when the bicuspid and tricuspid valves close. The swooshing sound is the regurgitation of blood into the atria. The cardiologist determined that the bicuspid valve was incompetent, resulting in abnormal blood flow on the left side of Stan's heart. Stan's difficulty breathing results from the abnormal blood flow caused by his incompetent valve. After reviewing the blood flow through the heart in this chapter, we are aware that blood entering the left atrium is returning from the lungs through the pulmonary veins. Because the bicuspid valve is incompetent, the pressure in the left atrium, which normally is low, increases substantially during ventricular contraction. The increased left-atrial pressure causes the pressure in the pulmonary veins and pulmonary capillaries to increase. As a result, fluid leaks from the pulmonary capillaries and accumulates in the lungs, causing pulmonary edema, making it difficult for Stan to breathe.

1. After reviewing figure 12.11*a*, we can see that the anterior interventricular artery supplies blood to the anterior wall of the heart and much of the left ventricle. A blocked anterior interventricular artery reduces the O_2 supply to the tissue and the cardiac muscle in that area of the heart is not able to contract effectively.
3. If the normal blood supply is reduced in a small area of the heart through which the left bundle branch passes, O_2 supply to the tissue, including the conducting system tissue, in the area is reduced and tissue function is reduced. The conduction of action potentials through that side of the heart is slowed or blocked. As a consequence, the left side of the heart contracts more slowly and its pumping effectiveness is reduced. Since the right bundle branch is not affected, the right side of the heart contracts more normally.
5. There are two different scenarios that we need to consider to answer this question. First, a person who has a damaged left bundle branch will exhibit

the consequences outlined for Apply It question 3, but we need to describe how the electrocardiogram will also be altered. We learned that the QRS complex results from depolarization of the ventricles after action potentials pass through the bundle branches to the Purkinje fibers. In this first scenario, action potentials pass through the right bundle branch normally but conduction of action potentials through the left bundle branch is slowed because of the damage. As a result, the QRS complex has an abnormal shape and it is prolonged.

In the second scenario, many ectopic action potentials arise in the atria. Ectopic action potentials originate in areas other than the SA node (the pacemaker of the heart). Each ectopic action potential initiates a new heartbeat, so we can predict that many ectopic action potentials cause an increase in heart rate. It is possible for some ectopic action potentials arising in the atria to occur while the ventricles are depolarized, but these action potentials do not initiate ventricular contraction. Therefore, there can be more P waves than QRS complexes in the electrocardiogram. If ectopic action potentials do not occur in a regular fashion, they can cause the heart to beat at an irregular rate, or arrhythmically.

7. Recall that the first heart sound occurs at the beginning of ventricular systole (contraction) and results from closure of the AV valves, and the second heart sound occurs at the beginning of ventricular diastole (relaxation) and results from closure of the semilunar valves. Most of the ventricular contraction occurs between the first and second heart sounds of the same beat. Between the first and second heart sounds, blood is ejected from the ventricles into the pulmonary trunk and the aorta. Between the second heart sound of one beat and the first heart sound of the next beat, the ventricles are relaxing and the semilunar valves are closed. No blood passes from the ventricles into the aorta or pulmonary trunk during that period.

9. In response to severe hemorrhage, blood pressure decreased, which is detected by baroreceptors. The decreased blood pressure leads to a reduced frequency of action potentials sent from the baroreceptors to the medulla oblongata. This causes the cardioregulatory center to increase sympathetic stimulation of the heart and increase the heart rate. Normally, sympathetic stimulation of the heart also increases stroke volume, as long as the volume of blood returned to the heart is optimizing ventricular stretching, or preload. Following hemorrhage, however, the blood volume in the body is reduced, and the venous return to the heart from the body is reduced. This leads to a

reduction in preload. According to Starling's law of the heart, as venous return and preload decrease, so does stroke volume. So, the heart rate is increased due to sympathetic stimulation, but the volume of blood returning to the heart is decreased; thus, the ventricle does not fill with blood. As a consequence, the stroke volume is low and the heart rate is high.

Chapter 13

Learn to Apply It

After reading Clinical Impact, "Circulatory Shock," in this chapter, we learned that circulatory shock is inadequate blood flow throughout the body and that septic shock is one type of circulatory shock. Septic shock results from infections that cause the release of toxic substances into the circulatory system that depress heart activity, cause vasodilation, and increase capillary permeability. We would expect that after T.J. developed septic shock, his blood volume would decrease as fluid moved from the more permeable capillaries into the interstitial spaces. The reduction in blood volume would lead to a drop in his blood pressure, stimulating the baroreceptor reflex mechanism and subsequently resulting in an increased heart rate. We would also expect T.J.'s stroke volume to decrease with a drop in blood volume. Increased sympathetic stimulation would cause vasoconstriction of blood vessels as T.J.'s body tried to maintain normal blood pressure. With the reduction in blood flow through his skin, T.J. would appear very pale. If T.J.'s blood pressure was not maintained, his blood pressure could continue to decrease to lethal levels.

1. As stated in the question, atherosclerosis of vessels occurs when lipid deposits block the vessels, which results in reduced blood flow through the vessel. The tissues to which the blocked vessels supply blood will therefore have reduced O_2 and nutrients. Since the carotid artery supplies blood to the brain, we would expect atherosclerosis of these vessels to lead to reduced brain function, which may include confusion and loss of memory.
3. The first condition to consider is why premature heartbeats result in a weak pulse. Premature beats of the heart result in the heart contracting before it has time to fill to its normal capacity. The volume of blood ejected from the heart will therefore be less causing a weak pulse. The second condition to consider is why would cardiovascular shock due to hemorrhage cause a weak pulse. Cardiovascular shock due to hemorrhage, or loss of large volumes of blood, will reduce the volume of blood returning to the heart. If this occurs, the stroke volume will also be greatly reduced since there is not as much blood to be pumped from the heart. Again, the low stroke volume leads to a weak pulse. The third condition to consider is why exercise causes a stronger pulse. Exercise causes an increase in heart rate and stroke volume. The increased stroke volume causes a stronger pulse.

5. While the student was sitting with her legs crossed, the blood vessels, particularly in the skin, were blocked. O_2 and nutrient levels decrease and waste products accumulate in tissues supplied by the blocked blood vessels. Recall that the precapillary sphincters that regulate blood flow through capillaries are regulated by metabolic needs, such as O_2 and nutrients. When these levels decrease, the precapillary sphincters relax allowing more blood flow through the tissues, and causing the appearance of the red blotch in the area that previously lacked blood flow.

7. The rapid loss of a large volume of blood activates the mechanisms responsible for maintaining blood pressure. Recall that blood pressure regulatory mechanisms include the baroreceptor reflexes, chemoreceptor reflexes, and hormonal mechanisms. In response to a dramatic drop in blood pressure due to the rapid loss of a large volume of blood, the baroreceptor mechanism, adrenal medullary mechanism, and chemoreceptor mechanism increase the heart rate and result in vasoconstriction of blood vessels, especially in the skin and viscera. Angiotensin II is produced quickly; it causes vasoconstriction and stimulates aldosterone secretion. Aldosterone, which requires up to 24 hours to become maximally active, increases water reabsorption from the kidneys and reduces the loss of water in the form of urine. Blood volume is therefore increased. All of these mechanisms increase blood pressure back to its normal value.

   If blood is lost over several hours, the decrease in blood pressure is not as dramatic as when blood loss occurs quickly. Consequently, mechanisms that respond to a rapid and large decrease in blood pressure are stimulated to a lesser degree. These include the chemoreceptor reflex, the vasopressin mechanism, and the adrenal medullary mechanism. The baroreceptor reflexes are most sensitive to sudden decreases in blood pressure, but the baroreceptor reflexes are still sensitive to decreases in blood pressure that occur over a period of several hours. The baroreceptor reflexes that trigger vasoconstriction in response to the blood loss are substantial. The kidneys detect even small decreases in blood volume. Consequently, the renin-angiotensin-aldosterone mechanism is activated and remains active until the blood pressure is returned to its normal range of values. Aldosterone secretion increases and, though it requires several hours to become maximally active, it continues to stimulate water reabsorption by the kidneys, increasing blood volume until the blood pressure returns to its normal range of values.

Chapter 14

Learn to Apply It

First, recall that vaccines are a form of artificial active immunity caused by deliberately introducing an antigen into the body, stimulating a primary response by the immune system. The immune system responds to the vaccine by increasing the number of specific memory cells and antibodies for the particular disease. This provides the long-lasting immunity without disease symptoms. The "booster" shot stimulates a memory (secondary) response, resulting in the formation of even more memory cells and antibodies. Because Shay will be exposed to more people at school, there is an increased chance that he will also be exposed to the particular pathogen. His "booster" shot increases his immune system's ability to fight the types of infections for which he was vaccinated.

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1. The function of lymphatic vessels is to return fluid from the peripheral tissues to the circulation. If lymphatic vessels are cut and tied, the movement of the fluid would be interrupted and edema will occur.
3. The first exposure to the disease-causing agent (antigen) evokes a primary immune response, which destroys the existing pathogens but also produces memory cells that can respond to future infections. As time passes, the antibodies produced during the primary immune response will degrade and memory cells will die. If, before all of the memory cells are eliminated, a second exposure to the antigen occurs, a secondary response results, increasing the number of antibodies and memory cells again. The newly produced memory cells could provide immunity until the next exposure to the antigen.

Chapter 15

Learn to Apply It

Mr. Theron suffers from emphysema, a respiratory disorder that results in the destruction of alveoli. This chapter explained that the alveoli form the respiratory membrane, the site of gas exchange between the atmosphere and the blood. Alveolar destruction would directly reduce the respiratory membrane surface and, therefore, gas exchange. As a consequence, Mr. Theron has exaggerated respiratory movements to compensate for the reduction in surface area. Blood Po_2 is an important stimulus for the respiratory center, and the increased respiratory movements keep the ventilation just adequate to maintain blood Po_2 in the low normal range. Because CO_2 diffuses across the respiratory membrane at a faster rate than O_2, the elevated respiration required to maintain blood Po_2 causes too much CO_2 to be expired, with the result that his blood Pco_2 level has dropped below normal. This chapter explained that a pneumothorax, or the introduction of air into the pleural cavity through an opening in the thoracic wall or lung, can cause a lung to collapse. Due to his emphysema, Mr. Theron's lung collapsed when alveoli near the surface of the lung ruptured, allowing air to enter the pleural space. The physician was able to diagnose Mr. Theron's collapsed lung by listening for respiratory sounds with a stethoscope. He detected respiratory sounds in the right lung but not in the left lung. We would expect Mr. Theron's respiratory movements to be even more exaggerated, since the respiratory membrane was reduced by one-half when his left lung collapsed. The reduction in the respiratory membrane would cause a drop in Po_2 and an increase in Pco_2, both of which would stimulate respiratory centers to increase ventilation. While in the hospital, Mr. Theron's breathing was assisted by a ventilator. If his emphysema continues to severely worsen, he may require a ventilator for the remainder of his life.

1. It could be that Jake was fibbing when he claimed to be unafraid, trying to impress his girlfriend. But whether he was frightened or not, in order for his body to produce such a sound, certain muscles need to contract. The muscles of expiration cause airflow from the lungs to the exterior through the larynx. As air rushes past the vocal cords, they vibrate. If air is explosively pushed past the vocal cords, they vibrate to a greater degree than when air is pushed past them to a lesser degree, and they produce a louder sound. As for the high

pitch of the scream, it is the position of the vocal cords that is important. More tension results in a higher frequency of vibration of the vocal cords, producing a higher-pitched sound. How does the tension increase? The arytenoid cartilages are rotated medially, which moves the vocal cords medially and posteriorly. Finally, the epiglottis-controlling muscles cause it to tip anteriorly so that air can flow past and out of the mouth. For Jake, the result was a high-pitched scream that either endeared him to his girlfriend or left him single.

3. The air the diver is breathing has a greater total pressure than atmospheric pressure at sea level. Consequently, the partial pressure of each gas in the air increases. According to Henry's law, as the partial pressure of a gas increases, the amount (concentration) of gas dissolved in the liquid (e.g., body fluids) with which the gas is in contact increases. When the diver suddenly ascends, the partial pressure of gases in the body returns toward sea level barometric pressure. As a result, the amount (concentration) of gas that can be dissolved in body fluids suddenly decreases. When the fluids can no longer hold all the gas, gas bubbles form.

5. When CO_2 moves from fetal blood into maternal blood, it increases CO_2 levels inside maternal red blood cells. As a result, pH inside maternal red blood cells decreases, the affinity of maternal hemoglobin for oxygen decreases, and more oxygen is released. Simultaneously, the movement of CO_2 from fetal blood into maternal blood decreases CO_2 levels inside fetal red blood cells and increases pH inside fetal red blood cells. This means that the affinity of fetal hemoglobin for oxygen increases, and more oxygen will bind to fetal hemoglobin. This effect increases the delivery of oxygen from maternal blood to fetal blood because maternal hemoglobin releases more oxygen and fetal hemoglobin is more effective at picking up that oxygen.

7. A person who cannot synthesize enzymes important for glucose metabolism inside their erythrocytes has mild erythrocytosis because his or her hemoglobin releases less oxygen to tissues. Consequently, increased erythropoietin will probably be released from the kidneys, and increased red blood cell production will occur in red bone marrow.

9. To answer this question, we need to consider what types of stimuli affect the respiratory center. Look at figure 15.16. Notice that receptors for temperature (e.g., cold water), pain (e.g., very cold water), and touch (e.g., swatting on the buttocks) all stimulate the respiratory center. That is why we gasp when we jump into a cold swimming pool—it is involuntary—and babies were swatted on the buttocks—to stimulate their first breath of air.

Chapter 16

Learn to Apply It

The first thing we learn is that Demondre is African-American and becomes uncomfortable after eating food with lactose. Next we learn that digestive enzymes are bound to the epithelial cells of the small intestine and that these enzymes are specific for certain nutrients, including lactose. Demondre's doctor tells him to avoid lactose because it gives him the symptoms that make him sick. We can conclude that Demondre has a problem with lactase, the enzyme that digests lactose. This isn't too surprising, since 80-90% of African-Americans synthesize lower quantities of lactase after childhood and cannot fully digest lactose. This condition is called lactose intolerance.

1. Four. Recall that the greater omentum is a localized mesentery, which consists of serous membranes. Each single layer of the mesentery has two layers of simple squamous epithelium. Since the greater omentum is folded back on itself, that results in 4 layers of simple squamous epithelium.
3. First, let's consider that acidic chyme in the small intestine is the stimulus. Stimuli are detected by receptors and then control centers send a signal to initiate a response that will regulate homeostasis. In this case, the control center is the pancreas. In response to the acidic chyme, pancreatic secretin stimulates bicarbonate ion secretion from the pancreas (the effector), which neutralizes the acidic chyme. Thus, secretin prevents the acid levels in the chyme from becoming too high, and keeps them in the normal range. The neutralization of the acidic chyme removes the stimulus for more secretin release and bicarbonate ion is no longer secreted. Because the response was inhibited, this is an example of a negative-feedback system.

5. Recall that diarrhea is either increased stool frequency or increased stool volume, which can result in the abnormal loss of fluid and ions from the colon. This fluid loss from the colon affects the cardiovascular system in the same way that blood loss does. In either case, the result is hypovolemia, which causes a drop in blood pressure in a positive-feedback cycle. Eventually heart failure results from insufficient blood flow to the heart itself.

Chapter 17

Learn to Apply It

Although Sadie's suggested snack did contain a lot of calories, which she and David needed for their day at the park, the food choices were not ideal. Most of the calories in the cookies and grape soda were simple sugars. Eating large amounts of simple sugars, as in Sadie's suggested snack, could result in large fluctuations in blood glucose levels. Though the children may initially have an increase in energy, they will most likely experience a drastic decrease in energy as well. Foods that include complex carbohydrates, such as those in the snack Sadie's mom suggested, have other nutrients, such as vitamins, many of which are necessary for normal metabolism. In addition, complex carbohydrates are digested and absorbed at a slower rate and do not contribute to drastic changes in blood glucose levels. Essentially, Sadie's mom selected food that would provide the children with energy and additional beneficial nutrients.

1. Most of the vitamins, with the exception of A, D, and niacin, are essential vitamins, meaning they cannot be produced by the body but must be obtained from the diet. Recall that after a vitamin is destroyed, its function is lost. If the vitamins were broken down by digestion before being absorbed, they would not be functional and vitamin deficiencies would occur.
3. Recall that the % Daily Values for energy-producing nutrients are based on a 2000 kcal/day diet. We can use the % Daily Values of a food on the Nutrition Facts food label to determine how the amounts of certain nutrients in the food fit into the overall diet. If a person consumes 1800 kcal/day, the % Daily Values will be reduced proportionally. To calculate the adjusted % Daily Values, the actual caloric intake (1800 kcal/day) should be divided by 2000 kcal/day. On a 1800 kcal/day diet, the total percentage of Daily Values for energy-producing nutrients should add up to no more than 90% because 1800/2000 = 0.9, or 90%.
5. We can see from table 17.1 that one cola or beer has about 145 kcal/serving. To determine the time it takes to burn these kilocalories we divide the kcal/serving by the number of kilocalories used per hour. Watching TV uses 95 kcal/h, so 145/95 is equal to about 1.5 hours, or 1 hour and 30 minutes. Jogging at a pace of 6 mph uses 580 kcal/h, so 145/580 is equal to 0.25 hours, or 15 minutes.

7. When blood vessels constrict, the flow of warm blood to the skin is reduced and the temperature of the skin is also reduced. The benefit is that less heat is lost through the skin to the environment and the internal body temperature is maintained. As the difference in temperature between the skin and the environment decreases, less heat is lost. If the skin temperature decreases too much, however, dilation of blood vessels to the skin occurs, which prevents the skin from becoming so cold that it is damaged.

Chapter 18

Learn to Apply It

First we learn that Maya is unable to retain water and is urinating excessively. This helps us to narrow our focus to kidney function. Next we learn that Maya has normal levels of ADH. Excessive urination falls under the category of diabetes (derived from the Greek for "siphon"); however, diabetes insipidus is a condition involving ADH abnormality. There are two main causes of diabetes insipidus: The posterior pituitary fails to secrete ADH, or the kidney tubules have abnormal receptors for ADH and do not respond to the presence of ADH. In people suffering from diabetes insipidus, much of the filtrate entering both the proximal and the distal convoluted tubules becomes urine. People with this condition can produce as much as 20-30 L of urine each day. Because they lose so much water, they are continually in danger of severe dehydration. Even though their urine is dilute, producing such a large volume of urine leads to the loss of Na+, Ca^{2+}, and other ions. The resulting ionic imbalances cause the nervous system and cardiac muscle to function abnormally. Because Maya's levels of ADH are normal, we can conclude that she has the type of diabetes insipidus involving abnormal receptors. Treatments for Maya include making sure she drinks plenty of water and giving her a sodium-sparing diuretic so that her kidneys retain sodium.

1. First, recall that the afferent arteriole supplies the glomerulus with blood to be filtered. The afferent arteriole has a larger diameter than the efferent arteriole. This means that blood enters the glomerulus at a faster rate than it exits, which causes blood in the glomerular capillaries to be under higher pressure than other capillary beds in the body. The high pressure in the glomerular capillaries is the driving force of filtration in the renal corpuscle. Thus, by changing the glomerular capillary pressure, the rate of filtration can be changed. Second, remember that arteriolar walls have a layer of smooth muscle and can vasoconstrict. If the afferent arteriole were to constrict, its diameter would be reduced, which would reduce the volume of blood entering the glomerulus. Reducing the volume of blood in the glomerulus reduces the pressure. Since more pressure equals more filtration, it follows that less pressure equals less filtration and therefore reduced urine production.
3. Reabsorption of water from the nephron is based on osmosis. If Na^+ and Cl^- are not actively transported out of the nephron, the concentration of ions

inside the nephron stays elevated. The normal osmotic gradient that moves water out of the nephron is greatly reduced and the water stays in the nephron, which increases urine volume.

5. Recall that the female urethra is much shorter than the male urethra and is more accessible to bacteria from the external environment. For this reason, females are more susceptible than males to cystitis.

7. Elevated blood CO_2 levels cause an increase in H^+ and a decrease in blood pH due to the following reaction:

$$CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows H^+ + HCO_3^-$$

However, the kidney also plays an important role in the regulation of blood pH. The kidney's rate of H^+ secretion into the urine and reabsorption of HCO_3^- increase. This helps prevent high blood H^+ levels and low blood pH in Adam.

Chapter 19

Learn to Apply It

In this chapter we learned that meiosis is cell division that produces haploid cells. When comparing meiosis in males and females, we find that the processes differ in several ways: in the stage in an individual's life when meiosis begins, in the types of cells produced, in the number of functional cells produced with each cell division, and in the stage of life when meiosis ceases to occur. In males, meiosis begins at puberty in the seminiferous tubules. Spermatogonia give rise to primary spermatocytes, which will undergo the process of meiosis. During this process, each primary spermatocyte eventually gives rise to four equal-sized mature sperm cells. Meiosis in females is more complex. The process actually begins before a female is even born. During fetal development, many of the oogonia in the ovaries degenerate. The remaining oogonia actually begin meiosis I and are called primary oocytes. At birth, the existing primary oocytes stop meiosis. After puberty and just before the ovulation of each oocyte, the primary oocyte that will be ovulated completes the first meiotic division to produce two different-sized cells: one large secondary oocyte and one small polar body. The secondary oocyte begins the second meiotic division but will complete the process only if fertilized by a sperm cell. In the case of fertilization, the secondary oocyte divides unevenly to form two cells. The smaller cell is another polar body and degenerates. In the larger cell, the haploid sperm nucleus combines with the haploid oocyte nucleus to form a zygote. So, in females, each primary oocyte produces only one large functional cell. The advantage of the size difference lies in the fact that sperm cells contribute only their DNA to the zygote; it is the oocyte that contributes cytoplasm and all the organelles to the zygote. In addition, one final difference between male and female meiosis is that in males, meiosis can continue until death and for females, the process of meiosis stops at menopause.

1. Recall that the prostate is inferior to the bladder and anterior to the rectum. Physicians can manually palpate the prostate through the wall of the rectum. The patient is fully awake and has relatively minor discomfort.
3. To make this prediction, recall that some forms of endocytosis are receptor-mediated. Also recall that viruses must enter their host cells to take over DNA replication and protein synthesis machinery. If the mechanism by which the virus is taken up by the host cell is understood, this mechanism could be

manipulated to prevent cancer from developing. It is well known that some human viruses induce the host cells to endocytose them by binding to certain cell surface receptors. By administering a blocker molecule (called an antagonist) that would bind to the cell surface receptor to prevent the virus from binding, endocytosis of the virus could not occur. Without endocytosis of the virus, it cannot replicate nor build new viruses. By administering both a blocker and a vaccine, a person would be doubly protected.

5. Molly's mother could have had leiomyomas also, although, without direct data from medical examinations, one cannot be certain. If that was the cause of her irregular menstruations, they may have become less frequent as Molly's mother experienced menopause. During menopause, the uterus gradually becomes smaller, and eventually the cyclical changes in the endometrial lining cease. If the condition was relatively mild, the onset of menopause could explain the gradual disappearance of the irregular and prolonged menstruations. (Note: If the tumors are large, constant and severe menstruations are likely even if regular menstrual cycles stop due to menopause.)

Chapter 20

Learn to Apply It

In this chapter we learned that the production of breast milk depends on a number of hormones. Estrogen and progesterone cause expansion of the duct system and the secretory units of the breast. Estrogen and progesterone levels during pregnancy prevent the breast from producing milk, but after parturition these hormone levels drop dramatically. Prolactin produced by the anterior pituitary stimulates milk production. We also learned that suckling stimulates the release of prolactin and oxytocin, which stimulates continued milk production and milk letdown. If Ming stops breastfeeding for a prolonged period of time, prolactin secretion will stop, which will cause milk production to decline. Ming can retain the capacity to breastfeed her baby by using a breast pump while she takes the prescribed medication. After finishing the antibiotic, Ming can then continue to breastfeed her baby.

1. To determine the days of the menstrual cycle when fertilization is most likely to occur, we need to remember the timing of ovulation, when the secondary oocyte is released from the ovary and available for fertilization. Recall that ovulation usually occurs around day 14 post-LMP. Also recall that sperm cells remain viable in the female reproductive tract for up to 6 days and that the secondary oocyte is capable of being fertilized for up to 1 day after ovulation. Considering all of these factors, we can conclude that fertilization would occur if sexual intercourse occurred between 5 days before ovulation and 1 day following ovulation. That will be between 10 days and 15 days post-LMP. You may find it interesting that data indicate that the most fertile period during the menstrual cycle is between 2 days just before ovulation and the day of ovulation.

3. Recall that clinical age is dependent on LMP (last menstrual period) of the mother and developmental age begins at fertilization, which is assumed to occur on day 14 after LMP. Most of the times reported in the text are developmental age. To determine the clinical age, add 14 to the developmental age. The one exception is parturition, which is reported as clinical age. To determine the developmental age, subtract 14 from the clinical age. We can easily construct a table to compare the ages:

	Clinical Age	Developmental Age
Fertilization	14 days	0 days

Implantation	21 days	7 days
Fetal period begins	70 days	56 days
Parturition	280 days	266 days

5. Genotypes are the alleles a person has for a given trait, and the phenotype is the person's appearance. In the case of polydactyly, there are three possible genotypes: DD (homozygous dominant), Dd (heterozygous), and dd (homozygous recessive). Since polydactyly is a dominant trait, we would expect the individuals with genotypes DD or Dd to exhibit polydactyly and the individuals with the genotype dd not to exhibit polydactyly.

Appendix F

Selected Abbreviations

α alpha
ACE angiotensin-converting enzyme
acetyl-CoA acetyl coenzyme A
ACh acetylcholine
ADH antidiuretic hormone
ADP adenosine diphosphate
ANH atrial natriuretic hormone
ANS autonomic nervous system
apo E apolipoprotein E
ATP adenosine triphosphate
AV atrioventricular beta
BCOP blood colloid osmotic pressure
BMI body mass index
BMR basal metabolic rate
BP blood pressure
BPG 2,3-bisphosphoglycerate
bpm beats per minute
BUN blood urea nitrogen
$C_6H_{12}O_6$ glucose
$Ca_{10}(PO_4)_6(OH)_2$ hydroxyapatite
Ca^{2+} calcium ion
cal calorie

cAMP cyclic adenosine monophosphate
CBC complete blood count
cGMP cyclic guanosine monophosphate
CH_3COOH acetic acid
Cl^- chloride ion
CNS central nervous system
CO cardiac output
CO carbon monoxide
CO_2 carbon dioxide
—COOH carboxyl group
COX-1 cyclooxygenase-1
CP capsule pressure
CRH corticotrophin-releasing hormone
CSF cerebrospinal fluid
DAG diacylglycerol
DNA deoxyribonucleic acid
ECG or EKG electrocardiogram
EEG electroencephalogram
EGF epidermal growth factor
ENS enteric nervous system
EPSP excitatory postsynaptic potential
FAD flavin adenine dinucleotide
$FADH_2$ reduced flavin adenine diphosphate
Fe^{2+} iron ion
FEV_1 forced expiratory volume in one second
FGF fibroblast growth factor
FSH follicle-stimulating hormone gamma
g gram
GABA gamma-aminobutyric acid
GCP glomerular capillary pressure

GDP guanosine diphosphate
GFR glomerular filtration rate
GH growth hormone
GHIH growth hormone-inhibiting hormone
GHRH growth hormone-releasing hormone
GnRH gonadotropin-releasing hormone
GTP guanosine triphosphate
H^+ hydrogen ion
H_2CO_3 carbonic acid
H_2O water
H_2O_2 hydrogen peroxide
H_2PO^- dihydrogen phosphate ion
HCG human chorionic gonadotropin
HCl hydrochloric acid
HCO_3^- bicarbonate ion
HDL high-density lipoprotein
Hg mercury
HIV human immunodeficiency virus
HLA human leukocyte antigen
HPO_4^{2-} monohydrogen phosphate ion
HR heart rate
I^- iodide ion
ICSH interstitial cell-stimulating hormone
IFP interstitial fluid pressure
Ig immunoglobulin
IP_3 inositol triphosphate
IPSP inhibitory postsynaptic potential
IU international units
K^+ potassium ion
kcal kilocalorie

kg kilogram
L liter
LDL low-density lipoprotein
LH luteinizing hormone
LHRH luteinizing hormone-releasing hormone
MAC membrane attack complex
MALT mucosa-associated lymphoid tissue
MAO monoamine oxidase
MAP mean arterial pressure
mEq milliequivalent
Mg^{2+} magnesium ion
MHC major histocompatibility complex
mOsm milliosmole
mRNA messenger ribonucleic acid
mV millivolt
Na^{+} sodium ion
NaCl sodium chloride
NAD^{+} nicotinamide adenine dinucleotide
NADH reduced nicotinamide adenine dinucleotide
$NaHCO_3$ sodium bicarbonate
NaOH sodium hydroxide
NFP net filtration pressure
$—NH_2$ amine group
NH_3 ammonia
NH_4^{+} ammonium ion
NK cells natural killer cells
NO nitric oxide
O_2 oxygen
OH^{-} hydroxide ion
PAH *para*-aminohippuric acid

P_{ALV} alveolar pressure
P_B barometric air pressure
PGE prostaglandin E
PGF prostaglandin F
P_i inorganic phosphate
PIF prolactin-inhibiting factor
PIH prolactin-inhibiting hormone
PIP_2 phosphoinositol
PMNs polymorphonuclear neutrophils
PNS peripheral nervous system
PO_4^{3-} phosphate ion
P_{PL} pleural pressure
PR peripheral resistance
PRF prolactin-releasing factor
PRH prolactin-releasing hormone
PTH parathyroid hormone
RANKL receptor for activation of nuclear factor kappa B ligand
RAS reticular activating system
RBC red blood count
RDA recommended daily allowances
RDI reference daily intake
RhoGAM Rh_o (D) immune globulin
RMP resting membrane potential
RNA ribonucleic acid
SA sinoatrial
SV stroke volume
T_3 triiodothyronine
T_4 tetraiodothyronine
TF tissue factor

TGF_β transforming growth factor beta

TMJ temporomandibular joint

TNF tumor necrosis factor

TRH thyroid-releasing hormone

TSH thyroid-stimulating hormone

V_A alveolar ventilation

VLDL very low-density lipoprotein

vWF von Willebrand factor

WBC white blood count

Prefixes, Suffixes, and Combining Forms

The ability to break down medical terms into separate components or to recognize a complete word depends on mastery of the combining forms (roots or stems) and the prefixes and suffixes that alter or modify their meanings. Common prefixes, suffixes, and combining forms are listed below in boldface type, followed by the meaning of each form and an example illustrating its use.

a-, an- without, lack of: *a*phasia (lack of speech), *an*aerobic (without oxygen)

ab- away from: *ab*ductor (leading away from)

-able capable: vi*able* (capable of living)

acou- hearing: *acou*stics (science of sound)

acr- extremity: *acro*megaly (large extremities)

ad- to, toward, near to: *ad*renal (near the kidney)

adeno- gland: *adeno*ma (glandular tumor)

-al expressing relationship: neur*al* (referring to nerves)

-algia pain: gastr*algia* (stomach pain)

angio- vessel: *angio*graphy (radiography of blood vessels)

ante- before, forward: *ante*cubital (before elbow)

anti- against, reversed: *anti*peristalsis (reversed peristalsis)
arthr- joint: *arthr*itis (inflammation of a joint)
-ary associated with: urin*ary* (associated with urine)
-asis condition, state of: homeost*asis* (state of staying the same)
auto- self: *auto*lysis (self breakdown)
bi- twice, double: *bi*cuspid (two cusps)
bio- live: *bio*logy (study of living)
-blast bud, germ: fibro*blast* (fiber-producing cell)
brady- slow: *brady*cardia (slow heart rate)
-c expressing relationship: cardia*c* (referring to heart)
carcin- cancer: *carcin*ogenic (causing cancer)
cardio- heart: *cardio*pathy (heart disease)
cata- down, according to: *cata*bolism (breaking down)
cephal- head: *cephal*ic (toward the head)
-cele hollow: blasto*cele* (hollow cavity inside a blastocyst)
cerebro- brain: *cerebro*spinal (referring to brain and spinal cord)
chol- bile: a*chol*ic (without bile)
cholecyst- gallbladder: *cholecyst*okinin (hormone causing the gallbladder to contract)
chondr- cartilage: *chondr*ocyte (cartilage cell)
-cide kill: bacteri*cide* (agent that kills bacteria)
circum- around, about: *circum*duction (circular movement)
-clast smash, break: osteo*clast* (cell that breaks down bone)
co-, com-, con- with, together: *co*enzyme (molecule that functions with an enzyme), *com*misure (coming together), *con*vergence (to incline together)
contra- against, opposite: *contra*lateral (opposite side)
crypto- hidden: *crypto*orchidism (undescended or hidden testes)
cysto- bladder, sac: *cysto*cele (hernia of a bladder)
-cyte-, cyto- cell: erythro*cyte* (red blood cell), *cyto*skeleton (supportive fibers inside a cell)

de- away from: *de*hydrate (remove water)
derm- skin: *derm*atology (study of the skin)
di- two: *di*ploid (two sets of chromosomes)
dia- through, apart, across: *dia*pedesis (ooze through)
dis- reversal, apart from: *dis*sect (cut apart)
-duct- leading, drawing: ab*duct* (lead away from)
-dynia pain: masto*dynia* (breast pain)
dys- difficult, bad: *dys*mentia (bad mind)
e- out, away from: *e*viscerate (take out viscera)
ec- out from: *ec*topic (out of place)
ecto- on outer side: *ecto*derm (outer skin)
-ectomy cut out: append*ectomy* (cut out the appendix)
-edem- swell: myo*edem*a (swelling of a muscle)
em-, en- in: *em*pyema (pus in), *en*cephalon (in the brain)
-emia blood: an*emia* (deficiency of blood)
endo- within: *endo*metrium (within the uterus)
entero- intestine: *enter*itis (inflammation of the intestine)
epi- upon, on: *epi*dermis (on the skin)
erythro- red: *erythro*cyte (red blood cell)
eu- well, good: *eu*phoria (well-being)
ex- out, away from: *ex*halation (breathe out)
exo- outside, on outer side: *exo*genous (originating outside)
extra- outside: *extra*cellular (outside the cell)
-ferent carry: af*ferent* (carrying to the central nervous system)
-form expressing resemblance: fusi*form* (resembling a fusion)
gastro- stomach: *gastro*dynia (stomach ache)
-genesis produce, origin: patho*genesis* (origin of disease)
gloss- tongue: hypo*gloss*al (under the tongue)
glyco- sugar, sweet: *glyco*lysis (breakdown of sugar)
-gram a drawing: myo*gram* (drawing of a muscle contraction)

-graph instrument that records: myo*graph* (instrument for measuring muscle contraction)

hem- blood: *hem*opoiesis (formation of blood)

hemi- half: *hemi*plegia (paralysis of half of the body)

hepato- liver: *hepa*titis (inflammation of the liver)

hetero- different, other: *hetero*zygous (different genes for a trait)

hist- tissue: *hist*ology (study of tissues)

homeo-, homo- same: *homeo*stasis (state of staying the same), *homo*logous (alike in structure or origin)

hydro- wet, water: *hydro*cephalus (fluid within the head)

hyper- over, above, excessive: *hyper*trophy (overgrowth)

hypo- under, below, deficient: *hypo*tension (low blood pressure)

-ia, -id expressing condition: neuralg*ia* (pain in nerve), flacc*id* (state of being weak)

-iatr- treat, cure: ped*iatr*ics (treatment of children)

-im not: *im*permeable (not permeable)

in- in, into: *in*jection (forcing fluid into)

infra- below, beneath: *infra*orbital (below the eye)

inter- between: *inter*costal (between the ribs)

intra- within: *intra*ocular (within the eye)

-ism condition, state of: dimorph*ism* (condition of two forms)

iso- equal, the same: *iso*tonic (same tension)

-itis inflammation: gastr*itis* (inflammation of the stomach)

-ity expressing condition: acid*ity* (condition of acid)

kerato- cornea or horny tissue: *kerat*inization (formation of a hard tissue)

-kin- move: *kin*esiology (study of movement)

leuko- white: *leuko*cyte (white blood cell)

-liga- bind: *liga*ment (structure that binds bone to bone)

lip- fat: *lip*olysis (breakdown of fats)

-logy study: histo*logy* (study of tissue)

-lysis breaking up, dissolving: glyco*lysis* (breakdown of sugar)
macro- large: *macro*phage (large phagocytic cell)
mal- bad: *mal*nutrition (bad nutrition)
malaco- soft: osteo*malac*ia (soft bone)
mast- breast: *mast*ectomy (excision of the breast)

mega- great: *mega*colon (large colon)
melano- black: *melano*cyte (black pigment-producing skin cell)
meso- middle, mid: *meso*derm (middle skin)
meta- beyond, after, change: *meta*stasis (beyond original position)
micro- small: *micro*organism (small organism)
mito- thread, filament: *mito*sis (referring to threadlike chromosomes during cell division)
mono- one, single: *mono*saccharide (one sugar)
-morph- form: *morph*ogenesis (formation of tissues and organs)
multi- many, much: *multi*nucleated (two or more nuclei)
myelo- marrow, spinal cord: *myelo*id (derived from bone marrow)
myo- muscle: *myo*cardium (heart muscle)
narco- numbness: *narco*tic (drug producing stupor or weakness)
neo- new: *neo*natal (first four weeks of life)
nephro- kidney: *nephr*ectomy (removal of the kidney)
neuro- nerve: *neur*itis (inflammation of a nerve)
oculo- eye: *oculo*motor (movement of the eye)
odonto- tooth or teeth: *odonto*my (cutting a tooth)
-oid expressing resemblance: epiderm*oid* (resembling epidermis)
oligo- few, scanty, little: *olig*uria (little urine)
-oma tumor: carcin*oma* (cancerous tumor)
-op- see, sight: my*op*ia (nearsighted)

ophthalm- eye: *ophthalm*ology (study of the eye)

ortho- straight, normal: *ortho*dontics (discipline dealing with the straightening of teeth)

-ory referring to: olfact*ory* (relating to the sense of smell)

-ose full of: adip*ose* (full of fat)

-osis a condition of: osteopor*osis* (porous condition of bone)

osteo- bone: *osteo*cyte (bone cell)

oto- ear: *oto*lith (ear stone)

-ous expressing material: ser*ous* (composed of serum)

para- beside, beyond, near to: *para*nasal (near the nose)

-pathy disease: cardio*pathy* (disease of the heart)

-penia deficiency: thrombocyto*penia* (deficiency of thrombocytes)

per- through, excessive: *per*meate (pass through)

peri- around: *peri*osteum (around bone)

-phag eat: dys*phag*ia (difficulty eating or swallowing)

-phas- speak, utter: a*phas*ia (unable to speak)

-phil- like, love: hydro*phil*ic (water-loving)

phleb- vein: *phleb*otomy (incision into a vein)

-phobia fear: hydro*phobia* (fear of water)

-plas- form, grow: neo*plas*m (new growth)

-plegia paralyze: para*plegia* (paralysis of lower limbs)

-pne- breathe: a*pne*a (lack of breathing)

pneumo- air, gas, or lungs: *pneumo*thorax (air in the thorax)

pod- foot: *pod*iatry (treatment of foot disorders)

-poie- making, production: hemato*poie*sis (make blood cells)

poly- many, much: *poly*cythemia (excess red blood cells)

post- after, behind: *post*partum (after childbirth)

pre-, pro- before, in front of: *pre*natal (before birth), *pro*sect (to cut before—for the purpose of demonstration)

procto- anus, rectum: *procto*scope (instrument for examining the rectum)

pseudo- false: *pseudo*stratified (falsely layered)

psycho- mind, soul: *psycho*somatic (effect of the mind on the body)

pyo- pus: *pyo*derma (pus in the skin)

re- back, again, contrary: *re*flect (bend back)

retro- backward, located behind: *retro*peritoneal (behind the peritoneum)

-rrhagia burst forth, pour: hemo*rrhage* (bleed)

-rrhea flow, discharge: rhino*rrhea* (nasal discharge)

sarco- flesh or fleshy: *sarco*ma (connective tissue tumor)

-sclero- hard: arterio*sclero*sis (hardening of the arteries)

-scope examine: endo*scope* (instrument for examining the inside of a hollow organ)

semi- half: *semi*lunar (shaped like a half moon)

somato- body: *somato*tropin (hormone causing body growth)

-stasis stop, stand still: hemo*stasis* (stop bleeding)

steno- narrow: *steno*sis (narrow canal)

-stomy to make an artificial opening: tracheo*stomy* (make an opening into the trachea)

sub- under: *sub*cutaneous (under the skin)

super- above, upper, excessive: *super*cilia (upper brows)

supra- above, upon: *supra*renal (above kidney)

sym-, syn- together, with: *sym*physis (growing together), *syn*apsis (joining together)

tachy- fast, swift: *tachy*cardia (rapid heart rate)

therm- heat: *therm*ometer (device for measuring heat)

-tomy cut, incise: phlebo*tomy* (incision of a vein)

tox- poison: anti*tox*in (substance that counteracts a poison)

trans- across, through, beyond: *trans*ection (cut across)

tri- three: *tri*ceps (three-headed muscle)

-troph- nourish: hyper*troph*y (enlargement or overnourishment)

-tropic changing, influencing: gonado*tropic* (influencing the gonads)

-uria urine: poly*uria* (excess urine)

vas- vessel : *vas*oconstriction (decreased diameter of blood vessel)

vene- vein: *vene*section (phlebotomy)

viscer- internal organ: *viscer*omotor (movement of internal organs)

zyg- yoked, paired: *zyg*ote (diploid cell)

GLOSSARY

Many of the words in this glossary and throughout the text are followed by a simplified phonetic spelling showing pronunciation. The pronunciation key reflects standard clinical usage, with minor modifications, as presented in *Stedman's Medical Dictionary* (27th edition), which has long been a leading reference volume in the health sciences.

abdomen (AB-doh-men) Belly, between the thorax and the pelvis.

abdominal cavity (ab-DOM-in-al) Space bounded by the diaphragm, the abdominal wall, and the pelvis.

abdominopelvic cavity (ab-DOM-ih-noh-PEL-vik) Abdominal and pelvic cavities considered together.

abduction (ab-DUK-shun) [abductio] Movement away from the midline.

absorption (ab-SORP-shun) The taking in or reception of gases, liquids, light, heat, or solutes, such as the movement of digested molecules across the intestinal wall and into the bloodstream; the movement of substances through the skin; and the movement of fluid into the lymphatics from the interstitial fluid.

accommodation (ah-kom-oh-DAY-shun) The act or state of adjustment or adaptation, such as the increase in the thickness and convexity of the lens of the eye in order to focus an object on the retina as the object moves closer to the eyes.

acetylcholine (AS-eh-til-KOH-leen)

Neurotransmitter substance released from motor neurons that innervate skeletal muscle fibers, all autonomic eganglionic neurons, all postganglionic parasympathetic neurons, some postganglionic sympathetic neurons, and some central nervous system neurons.

acetylcholinesterase (AS-eh-til-KOH-leen-ESS-ter-ase) Enzyme that breaks down acetylcholine to acetic acid and choline.

acetyl-CoA (AS-eh-til) Acetyl-coenzyme A; formed by the combination of the two-carbon acetyl group with coenzyme A; the molecule that combines with a four-carbon molecule to enter the citric acid cycle.

acid (ASS-id) Any substance that is a proton donor; or any substance that releases hydrogen ions.

acidosis (ass-ih-DOH-sis) Condition characterized by a lower than normal blood pH (pH of 7.35 or lower).

acinus (ASS-ih-nus), pl. **=acini** (ASS-ih-nai) [L., berry, grape] Grape-shaped secretory portion of a gland.

acromegaly (ak-roh-MEG-ah-lee) [G. *acro;*
megas, large] Disorder marked by progressive enlargement of the bones of the head, face, hands, feet, and thorax as a result of excessive secretion of growth hormone by the anterior pituitary gland.

acromion (ah-CROH-mee-on) [Fr. akron, tip + omos, shoulder] Lateral end of the spine of the scapula that projects as a broad, flattened process overhanging the glenoid fossa; articulates with the clavicle.

acrosome (AK-roh-sohm) [*acro,* tip + G. *soma,* body] A caplike organelle surrounding the anterior portion of a sperm cell, containing enzymes that facilitate entry of the sperm cell through the zona pellucida.

actin myofilament (AK-tin my-o-FIL-a-ment) One of the two major kinds of protein fibers that make up a sarcomere; thin

filaments; resemble two minute strands of pearls twisted together.

action potential All-or-none change in membrane potential in an excitable tissue that is propagated as an electrical signal.

activation energy Energy that must be added to atoms or molecules to start a chemical reaction.

active transport Carrier-mediated process that requires ATP and can move substances into or out of cells from a lower to a higher concentration.

adaptive immunity Immune system response in which there is an ability to recognize, remember, and destroy a specific antigen.

adduction (ah-DUK-shun) [L. *adductus*, to bring toward] Movement toward the midline.

adductor (ad-DUK-ter, -tor) [L. *adductus,* to bring toward] Muscle causing movement toward the midline.

adenoid (ADD-eh-noyd) Enlarged pharyngeal tonsil.

adenosine triphosphate (ah-DEN-o-seen try-FOS-fate) **(ATP)** Adenosine, an organic base, with three phosphate groups attached to it; energy stored in adenosine triphosphate is used in nearly all the energy-requiring reactions in the body.

ADH See *antidiuretic hormone.*

adipose (ADD-i-pose) [L. *adeps*, fat] Fat; relating to fat tissue.

adrenal cortex (ah-DREE-nal KOR-teks) The outer part of the adrenal gland, which secretes the following steroid hormones: glucocorticoids, mainly cortisol; mineralocorticoids, mainly aldosterone; and androgens.

adrenal gland (ah-DREE-nal) [L. *ad*, to; *ren*, kidney, near or on the kidneys] One of two endocrine glands located on the superior pole of each kidney; secretes the hormones epinephrine, norepinephrine, aldosterone, cortisol, and androgens.

adrenal medulla (ah-DREE-nal meh-DOO-lah) Inner part of the adrenal gland, which secretes mainly epinephrine but also small

amounts of norepinephrine.

adrenaline (ah-DREN-ah-lin) [from the adrenal gland] Synonym for *epinephrine.*

adrenocorticotropic hormone (ah-DREE-noh-KOR-tih-koh-TROH-pik) [L. *ad,* near + *ren*, kidney + *cortico*, cortex + *trophre*, nurture] **(ACTH)** Hormone of the anterior pituitary gland that stimulates the adrenal cortex to secrete cortisol.

adventitia (ad-ven-TISH-ah) [L. *adventicius,* coming from abroad or outside; foreign] Outermost covering of an organ that is continuous with the surrounding connective tissue.

aerobic respiration (ai-ROH-bik) Breakdown of glucose in the presence of oxygen to produce carbon dioxide, water, and approximately 38 ATP molecules; includes glycolysis, the citric acid cycle, and the electron-transport chain.

afferent (AF-eh-rent) [L. *afferens,* to bring to] Inflowing; conducting toward a center, denoting certain arteries, veins, lymphatics, and sensory nerves. Opposite of *efferent*.

afferent arteriole (ar-TEER-ee-ole) Small artery in the renal cortex that supplies blood to the glomerulus.

afferent fiber Sensory nerve fiber going from the peripheral to the central nervous system; sensory or afferent fiber.

afterload Resistance against which the ventricles must pump blood; it is increased in people who have hypertension.

agglutination (ah-glue-tih-NAY-shun) [L. *ad,* to + *gluten,* glue] Process by which cells stick together to form clumps.

agonist (AG-on-ist) [G. *agon,* a contest] Denoting a muscle in a state of contraction, with reference to its opposing muscle, or antagonist.

agranulocyte (ay-GRAN-you-loh-site) [G. *a-,* without + granular + *kytos,* cell] White blood cell with very small cytoplasmic

granules that cannot be easily seen with the light microscope; lymphocytes and monocytes.

aldosterone (al-DOS-ter-ohn) Steroid hormone produced by the adrenal cortex that facilitates potassium exchange for sodium in the distal convoluted tubule and collecting duct, causing sodium ion reabsorption and potassium and hydrogen ion secretion.

alkalosis (al-kah-LO-sis) Condition characterized by a higher than normal blood pH (pH of 7.45 or above).

alveolar duct (al-VEE-oh-lar) Part of the respiratory passages beyond a respiratory bronchiole; from it arise alveolar sacs and alveoli.

alveolar sac Two or more alveoli that share a common opening.

alveolus (al-VEE-oh-lus), pl. **alveoli** (al-VEE-oh-lie) [L., small cavity or hollow sac] Cavity; examples include the sockets into which the teeth fit and the ends of the respiratory system.

amino acid (ah-MEE-noh ASS-id) Class of organic acids containing an amine group (NH_2); the building blocks of proteins.

amniotic cavity (am-nee-OT-ik) [G. *amnios,* lamb] Fluid-filled cavity surrounding and protecting the developing embryo.

amylase (AM-il-eis) One of a group of starch-splitting enzymes that cleave starch, glycogen, and related polysaccharides.

anabolism (an-AB-oh-lizm) [G. *anabole,* a raising up] All the synthesis reactions that occur within the body; requires energy.

anaerobic respiration (an-uh-ROH-bik) Breakdown of glucose in the absence of oxygen to produce lactate and two ATP molecules; consists of glycolysis and the reduction of pyruvic acid to lactate.

anaphase (AN-uh-faze) [G. *ana,* up + *phases,* appearance] Stage of mitosis or meiosis in which the chromosomes move from the center area of the cell, the equatorial plane, toward the poles of the cell.

anatomical position (an-uh-TOM-i-kal) Position in which a person is standing erect with the feet facing forward, the arms hanging to the sides, and the palms of the hands facing forward.

anatomy (ah-NAT-oh-mee) [G. *ana,* apart + *tome,* a cutting] Scientific discipline that investigates the structure of the body.

androgen (AN-droh-jen) [G. *andros,* male] Hormone that stimulates the development of male sexual characteristics; includes testosterone.

anemia (ah-NEE-mee-ah) [G. *an,* without + *haima,* blood] Condition that results in less than normal hemoglobin in the blood or a lower than normal number of red blood cells.

anencephaly (AN-en-SEF-ah-lee) Defective development of the brain with absence of the cerebral and cerebellar hemispheres and with only a rudimentary brainstem.

angioplasty (AN-jee-oh-PLAS-tee) [G. *angio,* blood vessel] Technique used to dilate the coronary arteries by threading a small, balloonlike device into a partially blocked coronary artery and then inflating the balloon to enlarge the diameter of the vessel.

angiotensin (an-jee-oh-TEN-sin) [*angio,* blood vessel + *tensus,* to stretch] Angiotensin I is a peptide derived when renin acts on angiotensinogen; angiotensin II is formed from angiotensin I when angiotensin-converting enzyme acts on angiotensin I; angiotensin II is a potent vasoconstrictor, and it stimulates the secretion of aldosterone from the adrenal cortex.

angiotensinogen (an-jee-oh-TEN-sin-oh-jen) Protein found in the blood that gives rise to angiotensin I after renin, an enzyme secreted from the kidney, acts on it.

ANH See *atrial natriuretic hormone.*

antagonist (an-TAG-oh-nist) Muscle that works in opposition to another muscle.

anterior (an-TER-ee-or) [L., to go before] That which goes first; in humans, toward the belly or front.

anterior pituitary gland Portion of the pituitary gland derived from the oral epithelium.

antibody (AN-tih-body) [G. *anti,* against + *body,* a thing] Protein in the plasma that is responsible for antibody-mediated (humoral) immunity; binds specifically to an antigen.

antibody-mediated immunity Immunity resulting from B cells and the production of antibodies.

anticoagulant (AN-tee-koh-AG-you-lant) Chemical that prevents coagulation or blood clotting; an example is antithrombin.

antidiuretic hormone (an-tee-die-you-RET-ik) [G. *anti,* against + *uresis,* urine volume] **(ADH)** Hormone secreted from the posterior pituitary gland that acts on the kidney to reduce the output of urine; also called vasopressin.

antigen (AN-tih-jen) [G. *anti* (*body*) + *-gen,* a thing] Substance that induces a state of sensitivity or resistance to microorganisms or toxic substances after a latent period; substance that stimulates the adaptive immune system; self-antigens are produced by the body, and foreign antigens are introduced into the body.

antigen receptor Molecule on the surface of lymphocytes that specifically binds antigens.

aorta (ay-OR-tuh) [G. *aorte,* from + *aeiro,* to lift up] Large, elastic artery that is the main trunk of the systemic arterial system, which carries blood from the left ventricle of the heart and passes through the thorax and abdomen.

aortic semilunar valve Semilunar valve consisting of three cusps of tissue located at the base of the aorta where it arises from the left ventricle; the cusps overlap during ventricular diastole to prevent leakage of blood from the aorta into the left ventricle.

apex (AY-peks) [L., tip] Extremity of a conical or pyramidal structure; the apex of the heart is the rounded tip directed anteriorly and slightly inferiorly.

aphasia (ah-FAY-zee-ah) [G. *a-*, without + *phasis,* speech or speechlessness] Impaired or absent communication by speech,

writing, or signs because of dysfunction of brain centers in the dominant cerebral hemisphere.

apocrine (AP-oh-krin) [G. *apo,* away from + *krino,* to separate] Type of gland whose cells contribute cytoplasm to its secretion; sweat glands that produce organic secretions traditionally are called apocrine; however, these sweat glands are now known to be merocrine glands; see also *merocrine* and *holocrine.*

aponeurosis (ap-uh-noo-ROH-sis) [G. *neuron,* sinew; end of a muscle where it becomes a tendon] Sheet of fibrous connective tissue, or an expanded tendon, serving as the origin or insertion of a flat muscle.

apoptosis Programmed cell death; a normal process by which cell numbers within various tissues are adjusted and controlled.

appendicular (ah-pen-DIK-yoo-lar) [L. *appendo,* to hang something on] Relating to an appendage, such as the limbs and their associated girdles.

appendix (ah-ther-oh-skleh-ROE-tick), pl. **appendices** [L. *appendo,* to hang something on] Smaller structure usually attached by one end to a larger structure; a small blind extension of the colon attached to the cecum.

appositional growth (ap-oh-ZISH-uh-null) [L. *ap* + *pono,* to place at or to] To place one layer of bone, cartilage, or other connective tissue against an existing layer; increases the width or diameter of bones.

aqueous humor (AYK-wee-us) Watery, clear fluid that fills the anterior chamber and posterior chamber of the eye.

arachnoid mater (ah-RAK-noyd MA-ter) [G. *arachne,* spiderlike, cobweb] Thin, cobweblike meningeal layer surrounding the brain and spinal cord; the middle of three layers.

areola (ah-REE-oh-luh), pl. **areolae** (ah-REE-oh-lee) [small areas] Pigmented area surrounding the nipple of a mammary gland.

areolar (ah-REE-oh-lar) Relating to connective tissue with small spaces within it; loose connective tissue.

arrector pili (ah-REK-tor PIE-lee) [L., that which raises hair] Smooth muscle attached to the hair follicle and dermis that raises the hair when it contracts.

arteriole (ar-TEER-ee-ole) Minute artery with all three tunics that transports blood to a capillary.

arteriosclerosis (ar-TEER-ee-oh-skler-OH-sis) [L. *arterio-* + G. *sklerosis,* hardness] Hardness of the arteries.

artery (AR-ter-ee) [G. *arteria,* the windpipe] Blood vessel that carries blood away from the heart.

articulation (ar-tik-you-LAY-shun) [L. *articulatio,* a forming of vines] Place where two bones come together; a joint.

astrocyte (ASS-troh-site) [G. *astron,* star + *kytos,* a hollow cell] Star-shaped glial cell that helps regulate the composition of fluid around the neurons of the central nervous system; contributes to the blood-brain barrier.

atherosclerotic plaques (ah-ther-oh-skleh-ROT-ik) [G. *athere,* gruel or soft, pasty material + *sklerosis,* hardness] Lipid deposits in the tunica intima of large and medium-sized arteries.

atom (AT-om) [G. *atomos,* indivisible, uncut] Smallest particle into which an element can be divided using chemical methods; composed of neutrons, protons, and electrons.

atomic number (ah-TOM-ik) Number of protons in an element.

ATP See *adenosine triphosphate.*

atrial natriuretic (ay-TREE-al nay-tree-yoo-RET-ik) **hormone (ANH)** Hormone released from cells in the atrial wall of the heart when atrial blood pressure is increased; lowers blood pressure by increasing the rate of urine production.

atrioventricular (AV) bundle (AY-tree-oh-ven-TRIK-you-lar) Bundle of modified cardiac muscle fibers that projects from the AV node through the interventricular septum; conducts action potentials from the AV node rapidly through the interventricular septum; also called the bundle of His.

atrioventricular (AV) node Small collection of specialized cardiac muscle fibers located in the inferior part of the right atrium; delays action potential transmission to the atrioventricular bundle.

atrioventricular valve Valve between the atrium and the ventricle of the heart, the tricuspid valve between the right atrium and right ventricle, and the bicuspid (or mitral valve) between the left atrium and left ventricle.

atrium (AY-tree-um), pl. **atria** (AY-tree-ah) [L., entrance chamber] One of the two chambers of the heart that collect blood during ventricular contraction and pump blood into the ventricles to complete ventricular filling at the end of ventricular relaxation; the right atrium receives blood from the inferior and superior venae cavae and from the coronary sinus and delivers blood to the right ventricle; the left atrium receives blood from the pulmonary veins and delivers blood to the left ventricle.

auditory (AW-dih-tor-ee) Relating to hearing.

auditory ossicles (OS-ik-elz) Bones of the middle ear; the malleus, incus, and stapes.

auditory tube Air-filled passageway between the middle ear and pharynx.

auricle (AW-ri-kul) [L. *auris,* ear] Fleshy part of the external ear on the outside of the head; a small, conical pouch projecting from the upper anterior part of each atrium of the heart.

auscultatory (AW-skul-ta-to-ree) [L. *ausculto,* to listen] To listen to the sounds made by the various body structures, especially to Korotkoff sounds when determining blood pressure.

autocrine (AW-toh-krin) [G. *autos,* self + *krino,* to separate] Denoting self-stimulation through cellular production of a factor and a specific receptor for it.

autoimmune disease (aw-toh-im-YUNE) Disorder resulting from a specific immune system reaction against self-antigens.

autonomic nervous system (ANS) (awe-toh-NOM-ik) Part of the peripheral nervous system composed of efferent fibers that reach from the central nervous system to smooth muscle, cardiac muscle, and glands.

autorhythmicity (AW-toh-rith-mee-si-tee) Capacity to generate action potentials spontaneously.

autosome (AW-toh-zom) [G. *auto-*, self + *soma,* body] Any chromosome other than a sex chromosome; normally occurs in pairs in somatic cells and singly in gametes.

AV See *atrioventricular*.

axial (**AK**-see-al) [L. *axle,* axis] Head, neck, and trunk as distinguished from the extremities.

axon (AK-son) [G., axis] Main process of a neuron; usually conducts action potentials away from the neuron cell body.

baroreceptor (bar-oh-ree-SEP-ter) [G. *baro,* weight or pressure] Sensory nerve endings in the walls of the atria of the heart, aortic arch, and carotid sinuses; sensitive to stretching of the wall caused by increased blood pressure

baroreceptor reflex Process in which baroreceptors detect changes in blood pressure and produce changes in heart rate, force of heart contraction, and blood vessel diameter that return blood pressure toward normal levels.

basal nuclei Nuclei at the base of the cerebrum, diencephalon, and midbrain involved in controlling motor functions.

base Any substance that is a proton acceptor or any substance that binds to hydrogen ions; lower part or bottom of a structure; the base of the heart is the flat portion directed posteriorly and

superiorly; veins and arteries project into and out of the base, respectively.

basement membrane Structure that attaches most epithelia (exceptions include lymphatic vessels and the liver sinusoids) to underlying tissue; consists of carbohydrates and proteins secreted by the epithelia and the underlying connective tissue.

basilar membrane (BAS-ih-lar) One of two membranes forming the cochlear duct; supports the spiral organ.

basophil (BAY-so-fill) [G. *basis,* base + *phileo,* to love] White blood cell with granules that stain purple with basic dyes; promotes inflammation and prevents clot formation.

belly Largest part of a muscle between the origin and insertion.

benign (bee-NINE) [L. *benignus,* kind] Mild in character or nonmalignant; does not spread to distant sites.

beta-adrenergic (BAY-tah ad-re-NER-jik) **blocking agent** Drug that binds to and prevents adrenergic receptors from responding to adrenergic compounds that normally bind to beta-adrenergic receptors and cause them to function; beta-adrenergic blocking agents are used to treat certain arrhythmias in the heart and to treat tachycardia (rapid heart rate).

bicuspid valve (bi-KUS-pid) Valve closing the opening between the left atrium and left ventricle of the heart; has two cusps; also called the mitral valve.

bile (BYE-al) Fluid secreted from the liver, stored in the gallbladder, and released into the duodenum; consists of bile salts, bile pigments, bicarbonate ions, fats, and other materials.

bile salt Organic salt secreted by the liver that emulsifies lipids.

bilirubin (bill-ee-RU-bin) [L., bile + *ruber,* red] Bile pigment formed from the heme in hemoglobin during the destruction of red blood cells by macrophages.

biopsy (BIE-op-see) Process of removing tissue from living patients for diagnostic examination, or a specimen obtained by biopsy.

blastocele (BLAS-toe-seel) [G. *blastos,* germ + *koilos,* hollow] Cavity in the blastocyst.

blastocyst (BLAS-toh-sist) [G. *blastos,* germ + *kystis,* bladder] Early stage of mammalian embryo development consisting of a hollow ball of cells with an inner cell mass and an outer trophoblast layer.

blood-brain barrier Cellular and matrix barrier made up primarily of blood vessel endothelium, with some help from the surrounding astrocytes; it allows some (usually small) substances to pass from the circulation into the brain but does not allow other (larger) substances to pass.

blood group Category of red blood cells based on the type of antigen on the surface of the red blood cell; for example, the ABO blood group is involved with transfusion reactions.

blood pressure [L. *pressus,* to press] The force blood exerts against the blood vessel walls; expressed relative to atmospheric pressure and reported in the form of millimeters of mercury (mm Hg) of pressure.

bony labyrinth (LAB-ih-rinth) Interconnecting tunnels and chambers within the temporal bone in which the inner ear is located.

Bowman's capsule Enlarged end of the nephron; Bowman's capsule and the glomerulus make up the renal corpuscle.

brachial plexus (BRAY-kee-al) [L. *brachium,* arm] Nerve plexus to the upper limb; originates from spinal nerves C5 to T1.

brainstem Portion of the brain consisting of the midbrain, pons, and medulla oblongata.

breathing (BREE-thing) Movement of air into and out of the lung; see *ventilation*.

bronchiole (BRONG-key-ole) One of the finer subdivisions of the bronchial tubes, less than 1 mm in diameter, that has no cartilage in its wall but has relatively more smooth muscle and elastic fibers than do larger bronchial tubes.

bronchus (BRONG-kuss), pl. **bronchi** (BRONG-kigh) [G. *bronchos,* windpipe] Any one of the air ducts conducting air from the trachea to the bronchioles.

buffer (BUFF-er) Chemical that resists changes in pH when either an acid or a base is added to a solution containing the buffer.

burn Lesion caused by heat, acid, or other agents; a partial-thickness burn of the skin damages only the epidermis (first-degree burn) or the epidermis and part of the dermis (second-degree burn); a full-thickness (third-degree) burn destroys the epidermis and the dermis and sometimes the underlying tissue.

bursa (BURR-sah) [L., purse or pocket] Closed sac or pocket containing synovial fluid; usually found in areas where friction occurs.

calcaneus (kal-KAY-nee-us) [L., the heel] Largest tarsal bone forming the heel.

calcitonin (kal-sih-TONE-in) Hormone, released from cells of the thyroid gland, that acts on tissues, especially bone, to cause a decrease in blood levels of calcium ions.

calcium channel blocker (KAL-see-um) Class of drugs that specifically block channels in cell membranes through which calcium ions pass; calcium channel blockers are used to treat some kinds of cardiac arrhythmias.

callus (KAL-us) [L., hard skin] Thickening of the stratum corneum of skin in response to friction; the zone of tissue repair between fragments of a broken bone.

calorie (KAL-oh-ree) [L. *calor,* heat] Unit of heat or energy content; the quantity of energy required to raise the temperature of 1 gram of water 1°C. A Calorie (Cal), or kilocalorie (kcal), is the

amount of heat or energy required to raise the temperature of 1000 grams of water from 14°C to 15°C.

calyx (KAY-licks), pl. **calyces** (KAY-lih-sees) [G., flower petal or cup of a flower] Small container into which urine flows as it leaves the collecting ducts at the tip of the renal pyramids; the calyces come together to form the renal pelvis.

canaliculus (kan-ah-LIK-yoo-lus) Tiny canal in bone between osteocytes containing osteocyte cell processes; a cleftlike lumen between the cells of each hepatic cord, connects medial corner of the eye to the lacrimal sac.

cancer (KAN-ser) [L., a crab, suggesting crablike movement] Malignant neoplasm, or tumor.

capacitation (kuh-PAS-i-tey-shun) Process whereby the sperm cells develop the ability to fertilize oocytes.

capillary (KAP-ih-lair-ee) [L. *capillaris,* relating to hair, resembling a fine hair] Minute blood vessel consisting only of simple squamous epithelium and a basement membrane; major site for the exchange of substances between the blood and tissues.

carbohydrate (kar-boh-HIGH-drate) Organic molecule made up of one or more monosaccharides chemically bound together; sugars and starches.

carbon dioxide A molecular compound produced when cells synthesize ATP; expired as waste from lungs.

carbonic anhydrase (kar-BON-ik an-HIGH-drase) Enzyme that increases the rate at which carbon dioxide reacts with water to form hydrogen ions and bicarbonate ions.

carcinoma (kar-sih-NOH-mah) [G. *karkinoma,* cancer + *oma,* tumor] Malignant tumor derived from epithelial tissue.

cardiac cycle (KAR-dee-ak) One complete sequence of cardiac systole and diastole.

cardiac output Volume of blood pumped by either ventricle of the heart per minute; about 5 L/min for the heart of a healthy adult

at rest.

cardioregulatory center Specialized area within the medulla oblongata of the brain that receives sensory input and controls parasympathetic and sympathetic stimulation of the heart.

carotene (KAIR-oh-teen) Yellow pigment in plants such as squash and carrots; accumulates in the lipids of the stratum corneum and in the adipocytes of the dermis and subcutaneous tissue and is used as a source of vitamin A.

carotid bodies (kah-ROT-id) Small organs near the carotid sinuses that detect changes in blood oxygen, carbon dioxide, and pH.

carotid sinus Enlargement of the internal carotid artery near the point where the internal carotid artery branches from the common carotid artery; contains baroreceptors.

carpal (KAR-pal) [G. *karpos,* wrist] Associated with the wrist; bones of the wrist.

carrier molecule Protein that extends from one side of the cell membrane to the other; binds to molecules to be transported and moves them from one side of the cell membrane to the other.

cartilage (KAR-tih-lij) [L. *cartilage,* gristle] Firm, smooth, resilient, nonvascular connective tissue.

cascade (kas-KAID) [Fr. *cascare,* to fall] Series of sequential interactions, which once initiated continues to the final one; each interaction is activated by the preceding one, with cumulative effect.

catabolism (kah-TAB-oh-lizm) [G. *katabole,* a casting down] All the decomposition reactions that occur in the body; releases energy.

catalyst (KAT-uh-list) Substance that increases the rate of a chemical reaction; in the process, the catalyst is not permanently changed or used up.

cecum (SEE-kum) [L. *caecus,* blind] Blind sac forming the beginning of the large intestine.

cell (SELL) [L. *cella,* chamber] Basic unit of all plants and animals.

cell-mediated immunity Immunity resulting from the actions of T cells.

cell membrane Plasma membrane; outermost component of the cell, surrounding and binding the rest of the cell contents.

cellular respiration Process by which cells break down glucose or other molecules to synthesize ATP.

central canal Small canal containing blood vessels, nerves, and loose connective tissue and running parallel to the long axis of a bone; also called a haversian canal.

central nervous system (CNS) Brain and spinal cord.

centriole (SEN-tree-ole) Small organelle that divides and migrates to each pole of the nucleus during cell division; spindle fibers extend from the centromeres to the centrioles during mitosis.

centromere (SEN-tro-meer) [G. *kentron,* center + *meros,* part] Specialized region where chromatids are linked together in a chromosome.

cerebellum (ser-eh-BELL-um) [L., little brain] Part of the brain attached to the brainstem; important in maintaining muscle tone, balance, and coordination of movements.

cerebral aqueduct (SER-ee-bral) Small connecting tube through the midbrain between the third and fourth ventricles.

cerebrospinal fluid (SER-eh-broh-SPY-nal) (CSF) Fluid filling the ventricles and surrounding the brain and spinal cord.

cerebrum (ser-EE-brum) [L., brain] Largest part of the brain, consisting of two hemispheres and including the cortex, nerve tracts, and basal nuclei.

cerumen (seh-ROO-men) [L. *cera,* wax] Specific type of sebum produced in the external auditory canal; earwax.

cervical (SER-vih-kal) Neck.

cervical plexus Nerve plexus of the neck; originates from spinal nerves C1–C4.

cervix (SER-viks) [L., neck] Lower part of the uterus extending to the vagina.

chemical (KEM-ih-kal) Relating to chemistry, especially to the characteristics of atoms and molecules and to their interactions.

chemical bond Association between two atoms formed when the outermost electrons are transferred or shared between atoms.

chemical reaction Process by which atoms or molecules interact to form or break chemical bonds.

chemistry (KEM-uh-stree) [G. *chemeia,* alchemy] Science dealing with the atomic composition of substances and the reactions they undergo.

chemoreceptor reflex (kee-moh-ree-SEP-ter) Process in which chemoreceptors detect changes in oxygen levels, carbon dioxide levels, and pH in the blood and produce changes in heart rate, force of heart contraction, and blood vessel diameter that return these values toward their normal levels.

chemotaxis (kee-moh-TAK-sis) Attraction of cells to chemical stimuli.

cholecystokinin (KOH-leh-sis-toh-KIE-nin)[G. *chole,* bile + *kysis,* bladder + *kineo,* to move] (CCK) Hormone released from the duodenum; inhibits gastric acid secretion and stimulates contraction of the gallbladder.

chondrocyte (KON-droh-site) [G. *chondrion,* gristle + *cyte*] Cartilage cell.

chordae tendineae (KOR-dee ten-DIN-ee) [L., cord] Tendinous strands running from the papillary muscles to the free margin of the cusps that make up the tricuspid and bicuspid valves; prevent the cusps of these valves from extending up into the atria during ventricular contraction.

choroid (KOR-oid) [G. *chorioeides,* membranelike or lacy] Portion of the vascular tunic associated with the sclera of the eye; prevents scattering of light.

choroid plexus Specialized group of ependymal cells in the ventricles; secretes cerebrospinal fluid.

chromatid (KROH-mah-tid) [G. *chroma,* color] One of a pair of duplicated chromosomes, joined by the centromere, which separates from its partner during cell division.

chromatin (KROH-ma-tin) [G. *chroma,* color] Genetic material of the nucleus consisting of deoxyribonucleic acid (DNA) associated with proteins.

chromosome (KROH-moh-sohm) [G. *chroma,* color + *soma,* body] One of the bodies (normally 46 in humans) in the cell nucleus that carry the cell's genetic information.

chyle (KILE) [G. *chylos,* juice] Milky colored lymph with a high lipid content.

chylomicron (kye-lo-MY-kron) [*chylo-* + G. *micros,* small] Lipid droplet synthesized in the epithelial cells of the small intestine containing triglycerides, cholesterol, and lipoproteins.

chyme (KIME) [G. *chymos,* juice] Semifluid mass of partly digested food passed from the stomach into the duodenum.

ciliary body (SILL-ee-air-ee) [like an eyelash] Structure continuous with the choroid layer of the eye at its anterior margin that contains smooth muscle cells and is attached to the lens by suspensory ligaments; regulates the thickness of the lens and produces aqueous humor.

cilium (SILL-ee-um), pl. **cilia** (SILL-ee-ah) [L., eyelid] Mobile extension of a cell surface; varies from one to thousands per cell and contains specialized microtubules enclosed by the cell membrane.

citric acid cycle (SIT-rik) Series of chemical reactions in which citric acid (six-carbon molecule) is converted into a four-carbon molecule, carbon dioxide is formed, and energy is released; the

released energy is used to form ATP; the four-carbon molecule can combine with acetyl-CoA (two-carbon) to form citric acid and start the cycle again.

climacteric (KLI-mak-ter-ik) [G., the rung of a ladder] Period of endocrine, somatic, and transitory psychological changes occurring in the transition to menopause.

clitoris (KLIT-oh-ris) Small, erectile structure located in the anterior margin of the vestibule.

clot (KLOT) To coagulate; a soft, insoluble mass formed when blood coagulates.

clot retraction Condensation of the clot into a denser, more compact structure.

clotting factor One of many proteins found in the blood in an inactive state; activated in a series of chemical reactions that result in the formation of a blood clot.

coagulation (koh-ag-you-LAY-shun) Process of changing from a liquid to a solid, especially blood.

cochlea (KOK-lee-ah) Portion of the inner ear involved in hearing; shaped like a snail shell.

codon (KOH-don) Sequence of three nucleotides in mRNA that codes for a specific amino acid in a protein.

coenzyme (KOH-en-zaim) Substance that enhances or is necessary for the function of an enzyme.

collagen (KOL-ah-jen) [G. *koila,* glue + *gen,* producing] Ropelike protein of the extracellular matrix.

collecting duct Straight tubule that extends from the cortex of the kidney to the tip of the renal pyramid; filtrate from the distal convoluted tubules enters the collecting duct and is carried to the calyces.

colliculus (koh-LIK-yoo-lus) [L. *collis,* hill] One of four small mounds on the dorsal side of the midbrain; the superior two are

involved in visual reflexes, and the inferior two are involved in hearing.

colon (KOH-lon) Division of the large intestine that extends from the cecum to the rectum.

colostrum (koh-LOSS-trum) Thin, white fluid; the first milk secreted by the breast at the termination of pregnancy; contains less fat and lactose than the milk secreted later.

commissure (KOM-mih-shur) [L., a joining together] Bundle of nerve fibers passing from one side to the other in the brain or spinal cord.

common bile duct Duct formed by the union of the common hepatic and cystic ducts; it joins the pancreatic duct and empties into the duodenum.

common hepatic duct Duct formed by union of the right and left hepatic ducts; it joins the cystic duct to form the common bile duct.

compact bone Bone that is denser and has fewer spaces than spongy bone.

complement (KOM-pleh-ment) Group of serum proteins that stimulate phagocytosis, inflammation, and lysis of cells.

compound (KOM-pound) [to place together] Substance containing two or more different kinds of atoms that are chemically combined.

concha (KON-kah) [L., shell] Structure resembling a shell in shape; the three bony ridges on the lateral wall of the nasal cavity.

condyle (KON-dile) [G. *kondyles,* knuckle] Rounded, articulating surface of a joint.

cone Photoreceptor cell in the retina of the eye with cone-shaped photoreceptive process; important in color vision and visual acuity.

conjunctiva (kon-junk-TIE-vah) [L. *conjungo,* to bind together] Mucous membrane covering the anterior surface of the eye and the inner lining of the eyelids.

connective tissue One of the four major tissue types; consists of cells usually surrounded by large amounts of extracellular material; holds other tissues together and provides a supporting framework for the body.

constant region Part of an antibody that does not combine with an antigen and is the same in different antibodies; responsible for activating complement and binding the antibody to cells such as macrophages, basophils, and mast cells.

control center Structure that determines the set-point for a particular homeostatic mechanism; is often an area in the brain.

corn [L. *cornu,* horn] Thickening of the stratum corneum of the skin over a bony projection in response to friction or pressure.

cornea (KOR-nee-ah) [hornlike] Transparent, anterior part of the fibrous tunic of the eye, through which light enters the eye.

corneum (KOR-nee-um) See *stratum corneum*.

coronal plane (KOR-oh-nal) [G. *korone,* crown] Plane separating the body into anterior and posterior portions; also called a frontal plane.

coronary artery (KOR-oh-nair-ee) [circling like a crown] Artery that carries blood to the muscles of the heart; the left and right coronary arteries arise from the aorta.

coronary bypass Surgery in which a vein from another part of the body is grafted to a coronary artery in such a way as to allow blood flow past a blockage in the coronary artery.

coronary vein Vein that carries blood from the heart muscle, primarily to the right atrium.

corpus callosum (KOR-pus kah-LOH-sum) [L., body; callous] Large, thick nerve fiber tract connecting the two cerebral hemispheres.

corpus luteum (LOO-tee-um) Yellow endocrine body formed in the ovary in the site of a ruptured follicle immediately after ovulation; secretes progesterone and estrogen.

cortex (KOR-teks), pl. **cortices** (KOR-tih-sees) [L., bark] Outer part of an organ such as the brain, kidney, adrenal gland, or hair.

cortisol (KOR-tih-sol) Steroid hormone released by the adrenal cortex; increases blood glucose and inhibits inflammation; it is a glucocorticoid.

cotransport (koh-TRANS-port) Transport of one substance across a cell membrane, coupled with the simultaneous transport of another substance across the same membrane in the same direction.

covalent bond (koh-VAY-lent) Chemical bond formed when two atoms share one or more pairs of electrons.

coxal (KOK-sal) **bone** [L., hip] Also called hip bone.

cranial nerve (KRAY-nee-al) Peripheral nerve originating in the brain.

cranial vault Eight skull bones that surround and protect the brain; braincase.

cremaster muscle (kri-MAS-ter) Extension of abdominal muscles; in the male, it raises the testis.

crenation (kreh-NAY-shun) or (kree-NAY-shun) [L. *crena,* a notch] Cell shrinkage that occurs when water moves by osmosis from a cell into a hypertonic solution.

cretinism (KREH-tin-ism) Hypothyroidism in an infant; appears during the first years of life and results in stunting of body growth and mental development; hypothyroid dwarfism.

cricoid cartilage (CRY-koyd) Most inferior laryngeal cartilage.

cricothyrotomy (KRI-ko-thi-rot-o-mi) Formation of an artificial opening in a victim's air passageway through the membrane between the cricoid and thyroid cartilage.

crown (KROWN) Part of the tooth formed of and covered by enamel.

crypt (kript) [G. *kryptos,* hidden] Pitlike depression.

cryptorchidism (krip-TOR-kih-dizm) Failure of the testes to descend into the scrotal sac.

cupula (KOO-poo-lah) [L. *cupa,* a tub] Gelatinous mass that overlies the hair cells of the cristae ampullaris of the semicircular canals; responds to fluid movement.

cutaneous (kyu-TAY-nee-us) [L. *cutis,* skin] Relating to the skin.

cuticle (KEW-tih-cul) [L. *cutis,* skin] Outer thin layer, usually horny; for example, the outer covering of hair or the growth of the stratum corneum onto the nail.

cyanosis (sigh-ah-NOH-sis) [G., dark blue color] Blue coloration of the skin and mucous membranes caused by insufficient oxygenation of blood.

cystic duct (SIS-tik) Duct from the gallbladder; it joins the common hepatic duct to form the common bile duct.

cytoplasm (SIGH-toh-plazm) [G. *cyto,* cell + *plasma,* a thing formed] Cellular material surrounding the nucleus.

cytoskeleton (sigh-toh-SKEL-eh-ton) Collection of microtubules, microfilaments, and intermediate filaments that supports the cytoplasm and organelles; also involved with cell movements.

dartos muscle (DAR-toss) [Fr. *dero¯,* to skin] Layer of smooth muscle beneath the skin of the scrotum.

deciduous teeth (de-si-DEW-us) [L. *deciduus,* falling off] Primary teeth, which fall out to be replaced by the permanent teeth.

decomposition reaction (DEE-KOM-po-zishon) Breakdown of a larger molecule into smaller molecules, ions, or atoms.

deep [O.E. *deop,* deep] Away from the surface, internal.

defecation (def-eh-KAY-shun) [L. *defaeco,* to purify] Discharge of feces from the rectum.

deglutition (dee-glue-TISH-un) [L. *de-,* from, away + *glutio,* to swallow] Swallowing.

denaturation (dee-NAY-chur-AY-shun) Change in shape of a protein caused by breaking hydrogen bonds; agents that cause denaturation include heat and changes in pH.

dendrite (DEN-dright) [G. *dendrite,* tree] Short, treelike cell process of a neuron; receives stimuli.

dentin (DEN-tin) Bonelike material forming the mass of a tooth.

deoxyribonucleic (dee-OCK-see-RYE-boh-noo-KLEE-ik) **acid (DNA)** Type of nucleic acid containing the sugar deoxyribose; the genetic material of cells.

depolarize Decrease in the difference in potential (charge) between two points, as between the inside and outside of a cell membrane.

dermis (DER-miss) [G. *derma,* skin] Dense connective tissue that forms the deep layer of the skin; responsible for the structural strength of the skin.

desmosome (DEZ-moh-sohms) [G. *desmos,* a band + *soma,* body] Point of adhesion between two cells.

diabetes mellitus (die-ah-BEE-teez MEL-ih-tus) Condition resulting from too little insulin secreted from the pancreatic islets, insufficient numbers of insulin receptors on target cells, or defective receptors that do not respond to insulin.

diaphragm (DIE-ah-fram) [a partition wall] Muscular separation between the thoracic and abdominal cavities; its contraction results in inspiration.

diaphysis (die-AF-ih-sis) [G., growing between] Shaft of a long bone.

diastole (die-AS-toh-lee) [G. *diastole,* dilation] Relaxation of the heart chambers, during which they fill with blood; usually refers

to ventricular relaxation.

diastolic pressure Minimum arterial blood pressure achieved during ventricular diastole.

diencephalon (die-en-SEF-a-lon) [G. *dia,* through + *enkephalos,* brain] Part of the brain inferior to and nearly surrounded by the cerebrum and connecting posteriorly and inferiorly to the brainstem.

differentiation (DIF-er-en-SHEA-shun) The acquisition of specialized structures and functions different from the original structure and function.

diffusion (dih-FYU-zhun) [L. *diffundo,* to pour in different directions] Tendency for solute molecules to move from an area of higher concentration to an area of lower concentration in a solution; the product of the constant random motion of all atoms, ions, or molecules in a solution.

digestion (die-JEST-shun) Breakdown of carbohydrates, lipids, proteins, and other large molecules to their component parts.

digestive tract (die-JEST-iv) Tract from the mouth to the anus, including the stomach and intestines, where food is taken in, broken down, and absorbed.

digitalis (dij-i-TAL-is) [L., relating to fingerlike flowers] Steroid used in the treatment of heart diseases, such as heart failure; increases the force of contraction of the heart; extracted from the foxglove plant *(Digitalis purpura)*.

diploid (DIP-loyd) Condition in which there are 2 copies of each autosome and2 sex chromosomes (46 total chromosomes in humans).

disaccharidase (dye-SAK-er-id-ase) Enzyme that breaks disaccharides down to monosaccharides; commonly found in the microvilli of the intestinal epithelium.

disaccharide (die-SACK-ah-ride) [two sugars] Two monosaccharides chemically bound together; for example

glucose and fructose chemically join to form the disaccharide sucrose.

dissociate (DISS-so-see-ate) [L. *dis-* + *socio,* to disjoin, separate] Separation of positive and negative ions when they dissolve in water and are surrounded by water molecules.

distal (DISS-tal) [L. *di-* + *sto,* to be distant] Farther from the point of attachment to the body than another structure.

distal convoluted tubule Convoluted tubule of the nephron that extends from the ascending limb of the loop of Henle and ends in a collecting duct.

DNA See *deoxyribonucleic acid*.

dominant (DOM-ih-nant) [L. *dominus,* a master] In genetics, a gene that is expressed phenotypically to the exclusion of a contrasting recessive trait.

dorsal (DOR-sal) [L. *dorsum,* back] Back surface of the body; in humans, synonymous with *posterior*.

dorsal root Sensory root of a spinal nerve.

ductus arteriosus (DUK-tus ar-TEER-ee-oh-sus) Short artery that extends from the pulmonary trunk to the aorta; in the fetus, blood flows through the ductus arteriosus from the pulmonary trunk into the aorta and bypasses the lungs.

ductus deferens (DUK-tus DEH-fuh-renz) Duct of the testis, running from the epididymis to the ejaculatory duct; also called the vas deferens.

duodenum (du-oh-DEE-num) [L. *duodeni,* 12] First division of the small intestine; connects to the stomach.

dura mater (DYU-rah MAY-ter) [L., tough mother] Tough, fibrous membrane forming the outermost meningeal covering of the brain and spinal cord.

eardrum See *tympanic membrane*.

eccrine (EK-rin) [G. *ek,* out + *krino,* to separate] Exocrine; refers to water-producing sweat glands; see *merocrine*.

ECG See *electrocardiogram*.

ectoderm (EK-toe-derm) Outermost of the three germ layers of the embryo.

ectopic beat (ek-TOP-ik) Heartbeat that originates from an area of the heart other than the SA node.

edema (ee-DEE-mah) [G. *oidema,* a swelling] Excessive accumulation of fluid, usually causing swelling.

effector The component of a homeostatic mechanism that carries out an action to return the body to homeostasis—for example, the heart is an effector in blood pressure regulation.

efferent (EF-eh-rent) [L. *efferens,* to bring out] Conducting outward from a given organ or part, denoting certain arteries, veins, lymphatics, and motor nerves. Opposite of *afferent*.

efferent arteriole (ar-TEER-ee-ole) Vessel that carries blood from the glomerulus to the peritubular capillaries.

efferent ductule (DUCK-tool) Small duct that leads from the testis to the epididymis.

efferent fiber Nerve fiber going from the central nervous system toward the peripheral nervous system; motor fiber.

ejaculation (ee-JACK-you-LAY-shun) [to shoot out] Reflexive expulsion of semen from the penis.

ejaculatory duct (ih-JACK-you-leh-toh-ree) Duct formed by the union of the ductus deferens and the excretory duct of the seminal vesicle, which opens into the urethra.

electrocardiogram (ee-LEK-troh-KAR-dee-ohgram) (ECG) Graphic record of the heart's electrical currents obtained with an electronic recording instrument.

electrolyte (ee-LEK-troh-lite) [G. *electro,* + *lytos,* soluble] Positive and negative ions that conduct electricity in solution.

electron (ih-LEK-tron) Negatively charged particle around the nucleus of an atom.

electron-transport chain Series of energy-transfer molecules in the inner mitochondrial membrane; they receive energy and use it in the formation of ATP and water.

electronegativity The tendency of an atom to attract a bonding pair of electrons.

element (EL-ih-ment) [L. *elementum,* a rudiment] Simplest type of matter with unique chemical properties.

embolus (EM-boh-lus) [G. *embolos,* a plug] Detached clot or other foreign body that occludes a blood vessel.

embryo (EM-bree-oh) [Fr. *en,* in + *bryo¯,* to swell] In prenatal development, the developing human from the time of fertilization to approximately the end of the second month.

emission (ih-MISH-uhn) [L. *emissio,* to send out] Discharge; formation and accumulation of semen prior to ejaculation.

emulsification (ih-MUL-see-fi-ca-shun) Dispersal of one liquid, or very small globules of the liquid, within another liquid.

emulsify (eh-MUL-sih-fie) To form an emulsion, which is one liquid dispersed within another liquid.

enamel (ee-NAM-el) Hard substance covering hthe exposed portion of a tooth.

endocardium (EN-doh-KAR-dee-um) [G. *endon,* within + *kardia,* heart] Innermost layer of the heart, including endothelium and connective tissue.

endochondral ossification (en-doh-KON-dral osi-fi-KAY-shun) Bone formation within cartilage.

endocrine (EN-doh-krin) [*endo* + G. *krino,* to separate] Ductless gland that secretes internally, usually into the circulatory system.

endocytosis (EN-doh-sigh-TOH-sis) [*endo* + G. *kytos,* cell + *-osis,* condition] Bulk uptake of material through the cell membrane

by taking it into a vesicle.

endoderm (EN-doh-derm) [*endo* + G. *derma,* skin] Innermost of the three germ layers of the embryo.

endolymph (EN-doh-limf) [*endo* + G. *lympha,* clear fluid or springwater] Fluid inside the membranous labyrinth of the inner ear.

endometrium (en-doh-MEE-tree-um) [*endo* + G. *mē¯tra,* uterus] Mucous membrane that constitutes the inner layer of the uterine wall; consists of a simple columnar epithelium and a lamina propria that contains simple tubular uterine glands.

endomysium (EN-doh-MEE-see-um) (EN-doh-MIZ-ium) Fine connective tissue sheath surrounding a muscle fiber.

endoplasmic reticulum (EN-doh-PLAZ-mik reh-TIC-youlum) [*endo* + G. *plastos,* formed a network] Membranous network inside the cytoplasm; rough endoplasmic reticulum has ribosomes attached to the surface; smooth endoplasmic reticulum does not have ribosomes attached.

endosteum (en-DOSS-tee-um) [*endo* + G. *osteon,* bone] Membranous lining of the medullary cavity and the cavities of spongy bone.

endothelium, pl. **endothelia** (en-doh-THEE-lee-um) [G. *endo* + *thē¯lē¯,* nipple] Layer of flat cells lining especially blood and lymphatic vessels and the heart.

energy The capacity of an object to do work.

enteric nervous system (ENS) Complex network of neuron cell bodies and axons within the wall of the digestive tract; capable of controlling the digestive tract independently of the central nervous system through local reflexes.

enzyme (EN-zime) [G. *en,* in + *zyme,* leaven] Protein molecule that increases the rate of a chemical reaction without being permanently altered; an organic catalyst.

eosinophil (ee-oh-SIN-oh-fill) [eosin, an acidic dye + G. *phileo,* to love] White blood cell with granules that stain red with acidic dyes; participates in inflammatory responses of allergic reactions and asthma.

ependymal (ep-EN-dih-mal) Glial cell layer lining the ventricles of the brain.

epicardium (EP-ih-KAR-dee-um) [G. *epi,* upon + *kardia,* heart] Serous membrane covering the surface of the heart; also called the visceral pericardium.

epicondyle (ep-ih-KON-dile) [*epi* + G. *kondyle,* knuckle] Projection on (usually to the side of) a condyle.

epidermis (ep-ih-DER-miss) [*epi* + G. *derma,* skin] Outer portion of the skin formed of epithelial tissue that rests on the dermis; resists abrasion and forms a permeability barrier.

epididymis (EP-ih-DID-ih-miss) [*epi* + G. *didymos,* twin] Elongated structure connected to the posterior surface of the testis; site of storage and maturation of the sperm cells.

epiglottis (ep-ih-GLOT-is) [*epi* + G. *glottis,* the mouth of the windpipe] Plate of elastic cartilage, covered with mucous membrane, that serves as a valve over the opening of the larynx during swallowing to prevent materials from entering the larynx.

epimysium (ep-ih-MIS-ee-um) (ep-ih-MIZ-ee-um) [*epi* + G. *mys,* muscle] Fibrous connective tissue layer surrounding a skeletal muscle.

epinephrine (ep-ih-NEF-rin) [*epi* + G. *nephros,* kidney] Hormone similar in structure to the neurotransmitter norepinephrine; major hormone released from the adrenal medulla; increases cardiac output and blood glucose levels.

epiphyseal line (eh-pih-FIZ-ee-al) Dense plate of bone tissue in a bone that is no longer growing, indicating the former site of the epiphyseal plate.

epiphyseal plate Site at which bone growth in length occurs; located between the epiphysis and diaphysis of a long bone; area of cartilage where cartilage growth is followed by ossification; also called the growth plate.

epiphysis (eh-PIF-ih-sis) [*epi,* upon + G. *physis,* growth] End of a bone; separated from the remainder of the bone by the epiphyseal plate or epiphyseal line.

epiploic appendage (eh-pih-PLOH-ik) One of a number of little, fat-filled processes of peritoneum projecting from the serous coat of the large intestine.

episiotomy (eh-peez-ee-OT-oh-mee) [pubic region + G. *to¯me,* incision] Incision in the clinical perineum, sometimes performed during childbirth.

epithalamus (ep-ih-THAL-ah-mus) [G. *epi,* upon + thalamus] Small area of the diencephalon that is superior and posterior to the thalamus consists of the pineal gland and several small nuclei involved in the emotional and visceral responses to odors.

epithelial tissue (ep-ih-THEE-lee-al) One of the four major tissue types consisting of cells with a basement membrane (exceptions are lymphatic vessels and liver sinusoids), little extracellular material, and no blood vessels; covers the surfaces of the body and forms glands.

epithelium (ep-ih-THEE-lee-um) [G. *epi,* upon + *thele,* covering or lining] pl. **epithelia** (ep-ih-THEE-lee-ah) See *epithelial tissue.*

eponychium (ep-oh-NIK-ee-um) [G. *epi* + *onyx,* nail] Thin skin that attaches to the proximal part of the nail.

equilibrium (e-kwih-LIB-ree-um) [G. *aequus,* equal + *libra,* a balance] State created by a chemical reaction proceeding in opposite directions (e.g., from reactants to products and from products to reactants) at equal speed.

erection (ee-REK-shun) Engorgement of erectile tissue with blood, such as in the erectile tissues of the penis, causing the penis to enlarge and become firm.

erythrocyte (eh-RITH-roh-site) [G. *erythro,* red + *kytos,* cell] See *red blood cell.*

erythropoietin (eh-RITH-roh-POY-ee-tin) [*erythrocyte* + G. *poiesis,* a making] Protein hormone that stimulates red blood cell formation in red bone marrow.

essential amino acid amino acid, required by animals, that must be supplied in the diet.

esophagus (ee-SOF-ah-gus) [G. *oisophagos,* gullet] Part of the digestive tract between the pharynx and stomach.

estrogen (ES-troh-jen) Steroid hormone secreted primarily by the ovaries; involved in the maintenance and development of female reproductive organs, secondary sexual characteristics, and the menstrual cycle.

eustachian tube (you-STAY-shun) See *auditory tube.*

exchange reaction Combination of a decomposition reaction, in which molecules are broken down, and a synthesis reaction, in which the products of the decomposition reaction are combined to form new molecules.

exocrine (EK-soh-krin) [G. *exo-,* outside + *krino,* to separate] Gland that secretes to a surface or outward through a duct.

exocytosis (EK-so-sy-TOH-sis) Elimination of material from a cell through the formation of vesicles.

exophthalmia (ek-sof-THAL-me-ah) [G. *ex,* cut + *ophthalmos,* eye] Bulging of the eyes that frequently accompanies Graves disease, due to accumulation of a type of connective tissue behind the eye.

expiration (EKS-pih-RAY-shun) To breathe out; to move air out of the lungs.

extension [L. *extensio*] To stretch out, usually to straighten out a joint.

extracellular (eks-trah-SELL-you-lar) Outside of a cell.

extracellular matrix (MAY-triks) Nonliving chemical substances located between cells; often consists of protein fibers, ground substance, and fluid.

extrinsic muscle (eks-TRIN-sik) Muscle located outside of the structure on which it acts.

extrinsic regulation Regulation of the heart that involves mechanisms outside the heart, including nervous and hormonal regulation.

facet (FAS-et) [Fr., little face] Small, smooth articular surface.

facilitated diffusion (fah-SIL-ih-ta-ted di-FYOO-shun) Carrier-mediated process that does not require ATP and moves substances into or out of cells from a higher to a lower concentration.

fascia (FASH-ee-ah) [L., band or fillet] Loose areolar connective tissue beneath the skin (subcutaneous tissue), or dense connective tissue that encloses and separates muscles.

fasciculus (fah-SIK-you-lus) [L. *fascis,* bundle] Band or bundle of nerve or muscle fibers bound together by connective tissue.

fat Greasy, soft-solid lipid found in animal tissues and many plants; composed of glycerol and fatty acids.

fatty acid Straight chain of carbon atoms with a carboxyl group (–COOH) attached at one end; a building block of lipids.

feces (FEE-sees) Matter discharged from the digestive tract during defecation, consisting of the undigested residue of food, epithelial cells, intestinal mucus, bacteria, and waste material.

fertilization (FER-til-eye-ZAY-shun) Union of the sperm cell and oocyte to form a zygote.

fetus (FEE-tus) In prenatal development, the developing human between approximately 56 days and birth.

fibrillation (fih-brih-LAY-shun) Very rapid contraction of cardiac muscle fibers, but not of the muscle as a whole; results in

dramatically reduced pumping action of the heart.

fibrin (FIE-brin) [L. *fibra,* fiber] Threadlike protein fiber derived from fibrinogen by the action of thrombin; forms a clot—that is, a network of fibers that traps blood cells, platelets, and fluid—which stops bleeding.

fibrinogen (fie-BRIN-oh-jen) [L. *fibra,* fiber + *gen,* produce] Protein in plasma that gives rise to fibrin when acted on by thrombin to form a clot.

fibrinolysis (fih-bri-NOL-uh-sis) [L. *fibra,* fiber + G. *lysis,* dissolution] Breakdown of a clot by plasmin.

fibroblast (FIE-broh-blast) Cell in connective tissue responsible for the production of collagen.

filtrate Liquid that has passed through a filter—for example, fluid that enters the nephron through the filtration membrane of the glomerulus in the kidneys.

filtration (fil-TRAY-shun) Movement, resulting from a pressure difference, of a liquid through a filter, which prevents some or all of the substances in the liquid from passing.

filtration membrane Membrane formed by the glomerular capillary endothelium, the basement membrane, and the podocytes of Bowman's capsule.

fimbria (FIM-bree-ah), pl. **fimbriae** (FIM-bree-ee) Long, thin process that surrounds the opening of the uterine tube.

flagellum (fla-JELL-um), pl. **flagella** (fla-JELL-ah) [L., whip] Whiplike locomotor organelle similar to cilia except longer, and there is usually one per sperm cell.

flexion (FLEK-shun) [L. *flectus*] To bend.

focal point Point at which light rays cross after passing through a concave lens.

follicle-stimulating hormone (FOLL-ih-kull) **(FSH)** Hormone of the anterior pituitary gland that, in the female, stimulates the follicles of the ovary, assists in maturation of the follicle, and

causes secretion of estrogen from the follicle; in the male, it stimulates the epithelium of the seminiferous tubules and is partially responsible for inducing spermatogenesis.

fontanel (FON-tah-nel) [Fr., fountain] One of several membranous gaps between bones of the skull.

foramen (foh-RAY-men) Hole; referring to a hole or opening in a bone.

foramen ovale (oh-VAL-ee) In the fetal heart, the oval opening in the interatrial septum with a valve that allows blood to flow from the right to the left atrium, but not in the opposite direction; becomes the fossa ovalis after birth.

formed element Cell, such as a red blood cell or white blood cell, or cell fragments, such as a platelet, in blood.

fossa (FOSS-ah) Depression below the level of the surface of a bone; usually longitudinal in shape.

fovea centralis (FOH-vee-ah) Depression in the center of the macula of the eye; has the greatest visual acuity and only cones.

free energy Total amount of energy that can be liberated by the complete catabolism of food.

frenulum (FREN-you-lum) [L. *frenum,* bridle] Fold extending from the floor of the mouth to the middle of the undersurface of the tongue.

frontal plane Plane separating the body into anterior and posterior portions; also called a coronal plane.

FSH See *follicle-stimulating hormone.*

full-thickness burn Burn that destroys the epidermis and the dermis and sometimes the underlying tissue; sometimes called a third-degree burn.

fundus (FUN-dus) [L., bottom] Bottom, or area farthest from the opening, of a hollow organ, such as the stomach or the uterus.

gamete (GAM-eet) [G. *gametē̄s,* husband; *gametē̄,* wife] Germ cell, such as an oocyte or a sperm cell.

gamma globulin (GAM-ah GLOB-you-lin) Family of proteins found in plasma.

ganglion (GANG-lee-on), pl. **ganglia** (GANG-lee-ah) [G., knot] Group of neuron cell bodies in the peripheral nervous system.

gap junction Small channel that allows materials to pass from one cell to an adjacent cell; provides a means of intercellular communication.

gastric gland (GAS-trik) Gland within the stomach.

gastric inhibitory polypeptide Hormone released from the duodenum; inhibits gastric acid secretion.

gastrin (GAS-trin) Hormone secreted in the mucosa of the stomach and duodenum that stimulates secretion of hydrochloric acid by the gastric glands.

gastrointestinal tract (GAS-troh-in-TESS-tin-al) Technically, only the stomach and intestines. Often used as a synonym for *digestive tract,* which extends from the mouth to the anus.

gastrulation Phase of embryonic development involving the movement of epiblast cells and results in the formation of the three distinct germ layers.

gene Sequence of nucleotides in DNA that is a chemical set of instructions for making a specific protein.

gene expression Process whereby information stored in DNA directs protein synthesis; includes the processes of transcription and translation

genetics (jeh-NET-iks) Branch of science that deals with heredity.

genotype (JEN-oh-type) Genetic makeup of an individual.

GH See *growth hormone.*

giantism (JYE-an-tizm) Abnormal growth in young people because of hypersecretion of growth hormone by the pituitary gland.

gingiva (JIN-jih-vah) Dense fibrous tissue, covered by mucous membrane, that covers the alveolar processes of the upper and lower jaws and surrounds the necks of the teeth.

girdle (GIR-del) Bony ring or belt that attaches a limb to the body, such as the pectoral (shoulder) and pelvic girdles.

gland Single cell or multicellular structure that secretes substances into the blood, into a cavity, or onto a surface.

glial cells (GLEE-al) Cells of the nervous system other than neurons; play a support role in the nervous system; include astrocytes, ependymal cells, microglia, oligodendrocytes, and Schwann cells; also called neuroglia.

glomerulus (glo-MER-you-lus) [L. *glomus,* ball of yarn] Mass of capillary loops at the beginning of each nephron, nearly surrounded by Bowman's capsule.

glucagon (GLUE-kah-gon) [*glucose* + *ago¯,* to lead] Hormone secreted from the pancreatic islets of the pancreas that acts primarily on the liver to release glucose into the circulatory system.

glucocorticoid (glue-koh-KOR-tih-koyd) Hormone from the adrenal cortex capable of increasing the rate at which lipids are broken down to fatty acids and proteins are broken down to amino acids; elevates blood glucose levels and acts as an anti-inflammatory substance.

glucose A 6-carbon monosaccharide used by human cells for ATP synthesis among other functions.

glycerol (GLIS-er-ol) Three-carbon molecule with a hydroxyl group attached to each carbon; a building block of lipids.

glycogen (GLIE-koh-jen) Animal starch; composed of many glucose molecules bound together in chains that are highly branched; functions as a carbohydrate reserve; stores glucose molecules; in animal cells.

glycolysis (glye-KOHL-ih-sis) [G. *glykys,* sweet + *lysis,* a loosening] Anaerobic process during which one glucose

molecule is converted to two pyruvic acid molecules; a net of two ATP molecules is produced during glycolysis.

glycoprotein (glye-koh-PROH-teen) Organic molecule composed of a protein and a carbohydrate.

GnRH See *gonadotropin-releasing hormone.*

goblet cell Epithelial cell that has the end of the cell at the free surface distended with mucin.

goiter (GOY-ter) [L. *guttur,* throat] Enlargement of the thyroid gland, not due to a neoplasm, usually caused by a lack of iodine in the diet.

Golgi apparatus (GOL-jee) Named for Camillo Golgi, Italian histologist and Nobel laureate, 1843–1926. Stacks of flattened sacks, formed by membranes, that collect, modify, package, and distribute proteins and lipids.

gonad (GOH-nad) [L. *gonē,* seed] Organ that produces gametes; a testis or an ovary.

gonadotropin (GOH-nad-oh-TROH-pin) [*gonē,* seed + *trope,* a turning] Hormone capable of promoting gonadal growth and function; two major gonadotropins are luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

gonadotropin-releasing hormone (GnRH) Hypothalamic hormone that stimulates the secretion of LH and FSH from the anterior pituitary gland.

granulation tissue (gran-you-LAY-shun) Vascular connective tissue formed in wounds.

granulocyte (GRAN-you-loh-site) [*granular* + G. *kytos,* cell] White blood cell named according to the appearance, in stained preparations, of large cytoplasmic granules; neutrophils, basophils, and eosinophils.

Graves disease Type of hyperthyroidism resulting from abnormal proteins produced by the immune system that are similar in

structure and function to thyroid-stimulating hormone; often accompanied by exophthalmia.

growth hormone (GH) Protein hormone of the anterior pituitary gland; it promotes body growth, increases lipid mobilization, and increases blood glucose levels because it inhibits glucose utilization.

gynecomastia (GUY-nih-koh-MAS-tee-ah) Enlarged breasts in males.

gyrus (JIE-rus) [L. *gyros,* circle] Rounded elevation or fold on the surface of the brain.

hair Threadlike outgrowth of the skin, consisting of columns of dead, keratinized epithelial cells.

hair cell Cell of the inner ear containing hairlike processes (microvilli) that respond to bending of the hairs by depolarization.

haploid (HAP-loyd) Condition in which a cell has 1 copy of each autosome and 1 sex chromosome (23 total chromosomes in humans); characteristic of gametes.

haustra (HAW-strah) Sacs of the colon, formed by the teniae coli, which are slightly shorter than the gut, so that the gut forms pouches.

haversian canal (hah-VER-shan) Named for seventeenth-century English anatomist Clopton Havers (1650–1702). See *central canal*.

haversian system See *osteon*.

hCG See *human chorionic gonadotropin*.

heart-lung machine Machine that pumps blood and carries out the process of gas exchange; it substitutes for the heart and lungs during heart surgery.

heart rate Number of complete cardiac cycles (heartbeats) per minute.

heart transplant Process of taking a healthy heart from a recently deceased donor and transplanting it into a recipient who has a diseased heart.

heat Energy that results from the random movement of atoms, ions, or molecules; the greater the amount of heat energy in an object, the higher the object's temperature.

hematocrit (hee-MAT-oh-krit) [G. *hemato,* blood + *krino,* to separate] Percentage of total blood volume composed of red blood cells.

hematopoiesis (hee-MA-toh-poy-EE-sis) [G. *hemato,* blood + *poiesis,* a making] Production of blood cells.

hemidesmosome (HEM-ee-dez-moh-sohm) [G. *hemi,* one half] Half desmosome that occurs on the basal surface of epithelial cells that rest on the basement membrane.

hemoglobin (HEE-moh-GLOH-bin) [G. *hemato,* blood + *glob,* a ball] Red protein of red blood cells consisting of four globin proteins with an iron-containing red pigment, heme, bound to each globin protein; transports oxygen and carbon dioxide.

hemolysis (hee-MOL-ih-sis) [G. *hemo,* blood + *lysis,* destruction] Rupture of red blood cells.

hemolytic (hee-moh-LIT-ik) **disease of the newborn (HDN)** Destruction of red blood cells in the fetus or newborn, caused by antibodies produced in the Rh-negative mother acting on the Rh-positive blood of the fetus or newborn; also known as *erythroblastosis fetalis*.

hemorrhage (HEM-oh-raj) [G. *haima,* blood + *rhegnymi,* to burst forth] Rupture or leaking of blood from vessels.

hepatic (hep-AT-ik) [G. *hepar,* liver] Associated with the liver.

hepatic portal system [L. *porta,* gate] Blood flow through the veins that begin as capillary beds in the small intestine, spleen, pancreas, and stomach and carry blood to the liver, where they end as a capillary bed.

hepatic portal vein Vein that carries blood from the intestines, stomach, spleen, and pancreas to the liver.

Hering-Breuer reflex Named for German physiologist Heinrich E. Hering (1866–1948) and Austrian internist Josef Breuer (1842–1925). Process in which action potentials from stretch receptors in the lungs arrest inhalation; exhalation then occurs.

heterozygous (HET-er-oh-ZY-gus) Having two different genes for a given trait.

hilum (HIGH-lum) [L., a small amount or trifle] Part of an organ where the nerves and vessels enter and leave.

histology (his-TOL-oh-jee) [G. *histo,* web (tissue) + *logos,* study] Science that deals with the structure of cells, tissues, and organs in relation to their function.

holocrine (HOL-oh-kryn) [G. *holo,* whale + *krino,* to separate] Gland whose secretion consists of disintegrated cells of the gland; an example is a sebaceous gland.

homeostasis (hoh-mee-oh-STAY-sis) [G. *homoio,* like + *stasis,* a standing] Existence and maintenance of a relatively constant environment within the body with respect to functions and the composition of fluids and tissues.

homeostatic mechanism The sequence of events and set of structures involved in achieving homeostasis of a particular parameter.

homeotherm (HO-mee-oh-therm) [G. *homoiois,* like + *thermos,* warm] Any animal, including mammals and birds, that tends to maintain a constant body temperature; also referred to as warm-blooded.

homozygous (ho-moh-ZY-gus) Having two identical genes for a given trait.

hormone (HOR-mohn) [G. *hormon,* to set into motion] Substance secreted by endocrine tissues into the blood that acts on a target tissue to produce a specific response.

human chorionic gonadotropin (hCG) (koh-ree-ON-ik GOH-nad-oh-TROH-pin) Hormone, similar to LH, secreted from the placenta and essential for the maintenance of pregnancy for the first 3 months; prevents the corpus luteum from degenerating.

humoral immunity (HYU-mor-al im-YOU-nih-tee) See *antibody-mediated immunity.*

humoral stimulus A signal for hormone secretion. The concentration of various ions and nutrients in the blood determines the secretion of some hormones.

hydrophilic (hye-droh-FIL-ik) [G. *hydro,* water + *philos,* fond or loving] Attracting or associating with water molecules; tending to dissolve or associate with water molecules; tending to dissolve in water; polar.

hydrophobic (hye-droh-FOH-bik) [G. *hydro,* water + *phobos,* fear] Lacking affinity for water molecules; tending not to dissolve in water; nonpolar.

hydroxyapatite (hye-DROK-see-ap-ah-tyte) Complex crystal structure that makes up the mineral portion of bones and teeth.

hymen (HIGH-men) [G. *hymen,* membrane] Thin, membranous fold highly variable in appearance; partly occludes the opening of the vagina prior to its rupture; may occur for a variety of reasons and is frequently absent.

hyoid (HYE-oyd) [G., shaped like the letter epsilon, Îμ] U-shaped bone in the throat.

hypercapnia (HIGH-per-KAP-nee-ah) [*hyper* + G. *kapnos,* smoke, vapor] Abnormally increased arterial carbon dioxide tension or levels.

hyperpolarize (HYE-per-pol-lar-ize) [G. *hyper,* above + *polaris,* polar] To increase polarization of membranes of nerve or muscle cells.

hypertension (HIGH-per-TEN-shun) [G. *hyper,* above + *tensio,* tension] High blood pressure; generally, blood pressure greater than 140/90 is considered too high.

hyperthyroidism (high-per-THIGH-royd-ism) Abnormality of the thyroid gland in which thyroid hormone secretion is increased.

hypertonic (hye-per-TON-ik) [G. *hyper,* above + *tonos,* tension] Solution that causes cells to shrink.

hypodermis (high-poh-DER-miss) [G. *hypo,* under + *dermis,* skin] See *subcutaneous tissue.*

hypophysis (high-POF-ih-sis) [*hypo* + G., an undergrowth or growth] Endocrine gland attached to the hypothalamus by the infundibulum; the pituitary gland.

hypothalamic-pituitary portal system (HYE-poh-THAL-ah-mik pih-TOO-ih-terry) Series of blood vessels that carry blood from the area of the hypothalamus to the anterior pituitary gland; originates from capillary beds in the hypothalamus and terminates as a capillary bed in the anterior pituitary gland.

hypothalamus (high-poh-THAL-ah-muss) [*hypo* + G. *thalamos,* bedroom] Important autonomical and endocrine control center in the brain located beneath the thalamus.

hypothyroidism (high-poh-THIGH-royd-ism) Reduced secretion of thyroid hormones from the thyroid gland, leading to cretinism in infants and symptoms of inadequate thyroid hormone secretion in adults.

hypotonic (hye-poh-TON-ik) [*hypo,* under + G. *tonos,* tension or tone] Solution that causes cells to swell.

hypoxia (high-POK-see-ah) [*hypo* + oxygen] Below-normal levels of oxygen in arterial blood.

ICSH See *interstitial cell–stimulating hormone.*

Ig See *immunoglobulin.*

ileocecal junction (ILL-ee-oh-SEE-cal) Junction of the ileum of the small intestine and the cecum of the large intestine.

ileum (ILL-ee-um) [L. *eileo,* to roll up, twist] Third portion of the small intestine, about 3.5 meters in length; extends from the jejunum to the ileocecal opening.

immunity (im-YOU-nih-tee) Ability to resist damage from foreign substances, such as microorganisms, and harmful chemicals, such as toxins released by microorganisms.

immunoglobulin (IM-you-noh-GLOB-you-lin) **(Ig)** Antibodies.

implantation (im-plan-TAY-shun) Attachment of the blastocyst to the endometrium of the uterus; occurring 6 or 7 days after fertilization of the oocyte.

impotence (IM-poh-tence) Inability of the male to achieve or maintain an erection and thus engage in sexual intercourse.

incompetent valve Leaky valve; usually refers to a heart valve that allows blood to flow through it when it is closed.

incus (IN-cuss) [L., anvil] Middle bone of the middle ear; the anvil.

infarct (in-FARKT) Area of necrosis resulting from a sudden insufficiency of arterial blood supply.

inferior (in-FEE-ree-or) [L., lower] Down, or lower, with reference to the anatomical position.

inferior vena cava (VEE-nah KAY-vah) Receives blood from the lower limbs, pelvis, and abdominal organs and empties into the right atrium of the heart.

inflammatory (in-FLAM-ah-toh-ree) **response** Complex sequence of events, involving chemicals and immune system cells, that results in the isolation and destruction of foreign substances, such as bacteria; symptoms include redness, heat, swelling, pain, and disturbance of function.

infundibulum (IN-fun-DIB-you-lum) [L., a funnel] Funnel-shaped structure or passage—for example, the infundibulum that attaches the pituitary gland to the hypothalamus; funnel-like expansion of the uterine tube near the ovary.

inguinal canal (IN-gwin-al) Passageway through which a testis passes as it descends from the abdominopelvic cavity to the scrotum.

inguinal hernia (HER-nee-ah) Rupture that allows the potential protrusion of abdominal organs, such as the small intestine, through the inguinal canal.

innate immunity (IH-nate, ih-NATE) Immune system response that is the same on each exposure to an antigen; there is no ability to remember a previous exposure to a specific antigen.

inner cell mass Group of cells at one end of the blastocyst from which the embryo develops.

inorganic (in-or-GAN-ik) Molecules that do not contain carbon atoms; originally defined as molecules that came from nonliving sources; the original definition is no longer valid because carbon dioxide produced by living organisms is considered an inorganic molecule.

insertion (in-SIR-shun) The more movable attachment point of a muscle.

inspiration (in-spih-RAY-shun) To breathe in; to move air into the lungs, or inhale.

insulin (IN-syu-lin) Protein hormone, secreted from the pancreas, that increases the uptake of glucose and amino acids by most tissues.

interatrial septum (IN-ter-AY-tree-al) Cardiac muscle partition separating the right and left atria.

intercalated disk (in-TER-kah-lay-ted) [inserted between] Connection between cardiac muscle cells; important in coordinating the contractions of cardiac muscle cells; contains gap junctions that allow action potentials to pass from one cardiac muscle cell to adjacent cardiac muscle cells.

interferon (in-ter-FEER-on) Protein released by virally infected cells that binds to other cells and stimulates them to produce antiviral proteins that inhibit viral replication.

interkinesis (IN-ter-kye-NEE-sis) Short time period between the formation of the daughter cells of the first meiotic division and the second meiotic division.

interstitial cell (in-ter-STISH-al) Cell between the seminiferous tubules of the testes; secretes testosterone; also called Leydig cell.

interstitial cell–stimulating hormone (ICSH) Luteinizing hormone in males. Hormone of the anterior pituitary gland that stimulates the secretion of testosterone in the testes. See *luteinizing hormone.*

interventricular septum (IN-ter-ven-TRIK-you-lar) Cardiac muscle partition separating the right and left ventricles.

intestinal glands (in-TES-tin-al) Tubular glands in the mucous membrane of the small intestine.

intracellular (in-trah-SELL-you-lar) Inside a cell.

intramembranous ossification (IN-tra-MEM-bra-nus OS-ih-fih-KAY-shun) Bone formation within connective tissue membranes.

intramural plexus (in-trah-MYOO-ral PLEK-sus) [L., within the wall] Nerve plexus within the walls of the digestive tract; involved in local and autonomic control of digestion.

intrinsic factor (in-TRIN-sik) Factor secreted by the gastric glands and required for adequate absorption of vitamin B_{12}.

intrinsic muscle Muscle located within the structure on which it acts.

ion (EYE-on) Atom or group of atoms carrying an electrical charge because of a loss or gain of one or more electrons.

ionic bond (eye-ON-ik) Chemical bond resulting from the attraction between ions of opposite charge.

iris (EYE-ris) Specialized part of the vascular tunic of the eye; the "colored" part of the eye that can be seen through the cornea; consists of smooth muscles that regulate the amount of light entering the eye.

isometric contraction (eye-soh-MET-rik) Muscle contraction in which the length of the muscle does not change but the amount of tension increases.

isotonic (EYE-soh-TON-ik) [G. *iso,* equal + *tonos,* tension] Solution that causes cells to neither shrink nor swell.

isotonic contraction Muscle contraction in which the amount of tension is constant and the muscle shortens.

isotope (EYE-soh-tope) [G. *isos,* equal + *topos,* part] One of two or more elements that have the same number of protons and electrons but a different number of neutrons.

jaundice (JAWN-dis) [Fr. *jaune,* yellow] Yellowish staining of the skin, sclerae, and deeper tissues and excretions with bile pigments.

jejunum (je-JEW-num) [L. *jejunus,* empty] Portion of the small intestine, about 2.5 meters in length, between the duodenum and the ileum.

juxtaglomerular apparatus (JUKS-tah-gloh-MER-you-lar) [L. *juxta,* close to + *glomerulus*] Specialized wall of the distal convoluted tubule and afferent arteriole that secretes renin.

karyotype (KAIR-ee-oh-type) Display of chromosomes arranged by pairs.

keratin (KER-ah-tin) Protein that accumulates in cells of nails, hair, and the superficial layers of the epidermis of the skin.

keratinization (KER-ah-tin-i-ZAY-shun) Production of keratin and changes in the structure and shape of epithelial cells as they move to the skin surface.

kilocalorie (kcal) (KIL-oh-kal-oh-ree) Quantity of energy required to raise the temperature of 1 kg of water 1°C; 1000 calories;

equal to one dietary calorie.

kinetic (ki-NET-ik) [G. *kinetikos,* of motion] Relating to motion or movement.

Korotkoff sound (koh-ROT-kof) Named for Russian physician Nikolai Korotkoff (1874–1920). Sound heard over an artery when blood pressure is determined by the auscultatory method.

kyphosis (kie-FOH-sis) [G., humpback] Abnormal posterior curvature, or flexion, of the spine.

labia majora (LAY-bee-ah) Two rounded folds of skin surrounding the labia minora and vestibule.

labia minora Two narrow, longitudinal folds of mucous membrane enclosed by the labia majora; they unite anteriorly to form the prepuce.

labyrinth (LAB-ih-rinth) Series of membranous and bony tunnels in the temporal bone; the part of the inner ear involved in hearing and balance.

lacrimal ((LAK-rim-al) [L., a tear] Relating to tears or tear production.

lactation (lak-TAY-shun) [L. *lactatio,* suckle] Period following childbirth during which milk is formed in the breasts.

lacteal (LAK-tee-al) [relating to milk] Lymphatic vessel in the wall of the small intestine that carries chyle from the intestine and absorbs fat.

lacuna (la-KOO-nah), pl. **lacunae** (la-KOO-nee) [L., a pit] Small space, cavity, or depression; a space in cartilage in which a chondrocyte is located; a space in bone matrix in which an osteocyte is located; a cavity containing maternal blood in the placenta.

lamella (lah-MEL-ah), pl. **lamellae** (lah-MEL-ee) [L. *lamina,* plate, leaf] Thin sheet or layer of bone.

lamina (LAM-i-nah), pl. **laminae** (LAM-i-nay) [L. *lamina,* plate, leaf] Layer; a portion of the vertebra that extends from the

transverse process to the spinous process.

lamina propria (PROH-pree-ah) Layer of connective tissue underlying the epithelium of a mucous membrane.

lanugo (la-NYU-go) [L. *lana,* wool] Fine, soft fetal or embryonic hair.

laryngitis (lair-in-JIE-tis) Inflammation of the mucous membrane of the larynx.

laryngopharynx (lah-RING-oh-FAIR-inks) Part of the pharynx lying below the tip of the epiglottis extending to the level of the cricoid cartilage of the larynx.

larynx (LAIR-inks) Organ of voice production located between the pharynx and the trachea; it consists of a framework of cartilages and elastic membranes housing the vocal folds (true vocal cords) and the muscles that control the position and tension of these elements.

lateral [L. *latus,* side] Away from the middle or midline of the body.

lens Biconvex structure in the anterior part of the eye capable of being flattened or thickened to adjust the focus of light entering the eye.

leukemia (loo-KEE-mee-ah) [G. *leukos,* white + *haima,* blood] Tumor of the red bone marrow that results in the production of large numbers of abnormal white blood cells; often accompanied by decreased production of red blood cells and platelets.

leukocyte (LOO-koh-site) [G. *leukos,* white + *kytos,* cell] See *white blood cell.*

leukocytosis (LOO-koh-sigh-TOH-sis) [*leukocyte* + G. *-osis,* a condition] Higher than normal number of white blood cells.

leukopenia (loo-koh-PEE-nee-ah) [*leukocyte* + G. *penia,* poverty] Lower than normal number of white blood cells.

Leydig cell (LYE-dig) Named for German anatomist Franz von Leydig (1821–1908). See *interstitial cell.*

LH See *luteinizing hormone.*

ligament (LIG-ah-ment) Tough connective tissue band usually connecting bone to bone.

ligand (LIG-and, LIH-gand) [L. *ligo,* to bind] Molecule that binds to a macromolecule—for example, a ligand binding to a receptor.

limbic system (LIM-bic) [L. *limbus,* a border or boundary] Primitive part of the brain involved in visceral and emotional response and in the response to odor.

linea alba (LIN-ee-ah AL-bah) White line in the center of the abdomen where muscles of the abdominal wall insert.

lipase (LIE-pase) Enzyme that breaks down lipids.

lipid (LIP-id) [G. *lipos,* fat] Substance composed principally of carbon, oxygen, and hydrogen; generally soluble in nonpolar solvents; fats and cholesterol.

longitudinal section Cut made through the long axis of an organ.

loop of Henle U-shaped part of the nephron extending from the proximal to the distal convoluted tubule and consisting of descending and ascending limbs; many of the loops of Henle extend into the renal pyramids.

lordosis (lore-DOH-sis) [G., a bending backward; swayback] Abnormal anterior curvature of the spine, usually in the lumbar region; saddle back or swayback.

lumbosacral plexus (LUM-boh-SAY-kral) [L. *lumbus,* loin + *sacrum,* sacred] Nerve plexus that innervates the lower limbs; originates from spinal nerves L1–S4.

lunula (LOO-noo-lah) [L. *luna,* moon] White, crescent-shaped portion of the nail matrix visible through the proximal end of the nail.

luteinizing hormone (LH) (LOO-tee-in-eye-zing) Hormone of the anterior pituitary gland that, in the female, initiates final

maturation of the follicles, their rupture to release the oocyte, the conversion of the ruptured follicle into the corpus luteum, and the secretion of progesterone; in the male, it stimulates the secretion of testosterone in the testes and is sometimes referred to as interstitial cell–stimulating hormone (ICSH).

lymph (LIMF) [L. *lympha,* clear spring water] Clear or yellowish fluid derived from interstitial fluid and found in lymphatic vessels.

lymph node Encapsulated mass of lymphatic tissue found along lymphatic vessels; filters lymph and produces lymphocytes.

lymphatic nodule Small accumulation of lymph tissue lacking a distinct boundary.

lymphocyte (LIM-foh-site) [L. *lympho,* lymph + G. *kytos,* cell] Nongranulocytic white blood cell involved in the immune system; there are several types of lymphocytes with diverse functions, including antibody production, allergic reactions, graft rejections, tumor control, and regulation of the immune system.

lymphoma (lim-FOH-mah) Neoplasm (tumor) of lymphatic tissue that is almost always malignant.

lysis (LYE-sis) [G., dissolution or loosening] Rupturing or breaking of a cell membrane.

lysosome (LIE-soh-sohm) [G. *lysis,* a loosening + *soma,* body] Membrane-bound vesicle containing intracellular digestive enzymes.

macrophage (MAK-roh-fayj) [G. *makros,* large + *phago,* to eat] Large mononuclear, phagocytic cell.

macula (MAK-you-lah) [L., a spot] One of the sensory structures in the vestibule, consisting of hair cells and a gelatinous mass embedded with otoliths; responds to gravity. Also a small yellow spot in the posterior retina of the eye where the cones are concentrated; has no red tint because it is devoid of blood vessels.

major histocompatibility complex (MHC) molecules Glycoproteins found on the membranes of cells; MHC molecules serve as self-markers for the immune system and are used by antigen-presenting cells to present antigens to lymphocytes.

malignant (mah-LIG-nant) [L. *maligno,* to do anything malicious, with malice or intent to do harm] In reference to a neoplasm, the property of spreading locally and to distant sites.

malleus (MAL-ee-us) [L., hammer] Most lateral of the middle ear bones, attached to the tympanic membrane; the hammer.

mamma (MAM-ah) pl. **mammae** (MAM-ee) See *mammary gland*.

mammary gland (MAM-ah-ree) Organ of milk secretion, located in the breast, or mamma.

mastication (mas-tih-KAY-shun) [L. *mastico,* to chew] Chewing.

mastoid (MASS-toyd) [*mastos,* breast + *eidos,* resemblance] Resembling a breast—for example, the mastoid process of the temporal bone.

matrix (MAY-triks) Substance between the cells of a tissue.

matter Anything that occupies space.

mean arterial blood pressure Average of the arterial blood pressure; it is slightly less than the average of the systolic and diastolic blood pressure because diastole lasts longer than systole.

meatus (mee-AY-tus) [L., to go, pass] Passageway or tunnel.

meconium (meh-KOH-nee-um) [L. *mē̄kō̄n,* poppy] Greenish anal discharge from the fetus; consists of fluid swallowed, epithelial cells from the mucosa of the gut, mucus from the intestinal glands, and bile from the liver.

medial (MEE-dee-al) [L. *medialis,* middle] Toward the middle or midline of the body.

mediastinum (MEE-dee-ah-STIE-num) [L., middle septum or wall] Middle wall of the thorax, consisting of the trachea, esophagus,

thymus, heart, and other structures.

medulla (meh-DULL-ah) [L. *medius,* middle, marrow] Center, or core, of an organ, such as the adrenal gland, kidney, or hair.

medulla oblongata (ob-lon-GAH-tah) Inferior portion of the brainstem that connects the spinal cord with the brain; contains nuclei of cranial nerves plus autonomic control centers for heart rate, respiration, and so forth.

medullary cavity (MEH-dyu-lair-ee) Large, marrow-filled cavity in the diaphysis of a long bone.

medullary respiratory center (RES-pir-ah-TOR-ee) Nerve cells in the medulla oblongata and pons of the brain that control inspiration and expiration.

megakaryocyte (MEG-ah-KAIR-ee-oh-site) Large cell in red bone marrow that gives rise to platelets.

meiosis (my-OH-sis) [G., a lessening] Process of cell division that results in gametes. Consists of two cell divisions that result in four cells, each of which contains half the number of chromosomes as the parent cell; occur in the testes and ovaries.

melanin (MEL-ah-nin) [G. *melas,* black] Brown to black pigment responsible for skin and hair color.

melanocyte (MEL-an-oh-syte) [G. *melas,* black + *kytos,* cell] Cells, found mainly in the stratum basale of skin, that produce the brown or black pigment melanin.

melanocyte-stimulating hormone (MSH) (MEL-an-oh-syte) [G. *melas,* black + *kytos,* cell] Peptide hormone secreted by the anterior pituitary gland; increases melanin production by melanocytes, making the skin darker in color.

melanoma (MEL-ah-NOH-mah) [G. *melas,* black + *oma,* tumor] Malignant tumor derived from melanocytes.

melanosome (MEL-ah-no-sohm) [G. *melano,* black + *soma,* body] Pigment granule produced by melanocytes.

melatonin (mel-ah-TONE-in) Hormone secreted by the pineal gland; may inhibit gonadotropin-releasing hormone secretion from the hypothalamus.

membrane-bound receptor Receptor molecule, such as a hormone receptor, that is bound to the plasma membrane of the target cell.

membranous labyrinth (MEM-brah-nus LAB-ih-rinth) Membrane-bound set of tunnels and chambers of the inner ear.

memory cell Lymphocyte derived from a B cell or T cell that has been exposed to an antigen; when exposed to the same antigen a second time, the memory cell rapidly responds to provide immunity.

menarche (me-NAR-key) [G. *mē¯n,* month + *archē¯,* beginning] First menstrual period or flow.

meninges (meh-NIN-jeez) [G. *meninx,* membrane] Series of three connective tissue membranes: the dura mater, arachnoid mater, and pia mater; they surround and protect the brain and spinal cord.

menopause (MEN-oh-paws) [L. *mē¯n,* month + *pausis,* cessation] Permanent cessation of the menstrual cycle.

menses (MEN-seez) [L. *mensis,* month] Loss of blood and tissue as the endometrium of the uterus sloughs away at the end of the menstrual cycle; occurring at about 28-day intervals in the nonpregnant female of reproductive age.

menstrual cycle (MEN-stru-al) Series of changes that occur in sexually mature, nonpregnant females and result in menses; specifically includes the cyclical changes that occur in the uterus and ovary.

merocrine (MARE-oh-krin) [G. *meros,* part + *krino,* to separate] Gland that secretes products with no loss of cellular material; an

example is water-producing sweat glands; see *apocrine* and *holocrine.*

mesentery (MESS-en-ter-ree) [G. *mesos,* middle + *enteron,* intestine] Double layer of peritoneum extending from the abdominal wall to the abdominopelvic organs; conveys blood vessels and nerves to abdominopelvic organs; holds and supports abdominopelvic organs.

mesoderm (MEZ-oh-derm) Middle of the three germ layers of the embryo.

mesovarium (MEZ-oh-VAR-e-um) Mesentery of the ovary; mesentery that attaches the ovary to the posterior surface of the broad ligament.

messenger ribonucleic acid (mRNA) Type of RNA that moves out of the nucleus and into the cytoplasm, where it is used as a template to determine the structure of proteins.

metabolic rate Total amount of energy produced and used by the body per unit of time.

metabolism (meh-TAB-oh-lizm) [G. *metabole,* change] Sum of the chemical changes that occur in tissues, consisting of the breakdown of molecules (catabolism) to produce energy and the buildup of molecules (anabolism), which requires energy.

metaphase (MET-ah-fayz) [G. *meta,* after + *phasis,* an appearance] Stage of mitosis or meiosis in which the chromosomes become aligned near the center of the cell, at the equatorial plane, separating the centromeres, or chromosome pairs (see also *meiosis*). The centromeres of each chromosome divide, and the two daughter chromosomes are directed toward opposite poles of the cell.

metastasis (meh-TAS-tah-sis) Shifting of a disease or a neoplasm from one part of the body to another remote from the original location.

micelle (mi-SEL, my-SEL) [L. *micella,* small morsel] Droplet of digested lipid surrounded by bile salts in the small intestine.

microglia (my-KROH-glee-ah) [G. *micro,* small + *glia,* glue] Small neuroglial cells that become phagocytic and mobile in response to inflammation; considered to be macrophages of the central nervous system.

microtubule (my-kroh-TOO-bule) Hollow tube composed of tubulin; microtubules help support the cytoplasm of the cell and are components of certain cell organelles, such as cilia and flagella.

microvillus (my-kroh-VIL-us), pl. **microvilli** (my-kroh-VIL-eye) One of the minute projections of the cell membrane that greatly increase the surface area of the cell membrane.

micturition reflex (mik-choo-RISH-un) Contraction of the urinary bladder stimulated by stretching of the urinary bladder wall; it results in emptying of the urinary bladder.

midbrain Superior end of the brainstem; located between the pons and diencephalon; contains fibers crossing from the brain to the spinal cord and vice versa, as well as nuclei and visual reflex centers.

midsagittal (MID-SAJ-i-tal) Plane running vertically through the body and dividing it into equal right and left parts.

mineral (MIN-er-al) Inorganic nutrient necessary for normal metabolic functions.

mineralocorticoid (MIN-er-al-oh-KOR-tih-koyd) Steroid hormone released from the adrenal cortex; acts on the kidney to increase the rate of sodium ion reabsorption from the nephron and potassium and hydrogen ion secretion into the nephron of the kidney; an example is aldosterone.

mitochondrion (my-toe-KON-dree-on), pl. **mitochondria** (my-toe-KON-dree-ah) [G. *mitos,* thread + *chandros,* granule] Small, spherical, rod-shaped or thin filamentous structure in the cytoplasm that is a major site of ATP production.

mitosis (my-TOH-sis) [G., thread] Division of the nucleus. Process of cell division that results in two daughter cells with exactly the

same number and type of chromosomes as the parent cell.

mitral valve (MY-tral) [resembling a bishop's miter, a two-pointed hat] See *bicuspid valve.*

molecule (MOLL-eh-kyul) Two or more atoms chemically combined to form a structure that behaves as an independent unit.

monocyte (MON-oh-site) [G. *mono,* one or single + *kytos,* a cell] Type of white blood cell that transforms to become a macrophage.

mononuclear phagocytic system (mon-oh-NOO-klee-ar fag-oh-SIT-ik) Phagocytic cells with a single nucleus, derived from monocytes; the cells either enter a tissue by chemotaxis in response to infection or tissue damage or are positioned to intercept microorganisms entering tissues.

monosaccharide (MON-oh-SACK-ah-ride) Basic building block from which more complex carbohydrates are constructed—for example, glucose and fructose.

mons pubis (MONZ PYU-bis) [L., mountain] Prominence formed by a pad of adipose tissue over the pubic symphysis in the female.

morula (MOR-you-lah) [L. *morus,* mulberry] Solid mass of cells resulting from the early cleavage divisions of the zygote.

motor neuron Neuron in the brain or spinal cord that innervates skeletal, smooth, or cardiac muscle cells or glands. Somatic motor neurons directly innervate skeletal muscle cells. Two autonomic motor neurons in series extend from the central nervous system to smooth or cardiac muscle cells or glands.

motor unit Single motor neuron and all the skeletal muscle fibers it innervates.

MSH See *melanocyte-stimulating hormone.*

mucin (MYU-sin) Secretion containing mucopolysaccharides (proteoglycans), produced by mucous gland cells.

mucosa (myu-KOH-sah) [mucus-producing membrane] Mucous membrane consisting of the epithelium and connective tissue; in the digestive tract, there is also a layer of smooth muscle.

mucous membrane (MYU-kus) Thin sheet consisting of epithelium and connective tissue that lines cavities opening to the outside of the body; many contain mucous glands, which secrete mucus.

mucus (MYU-kus) Viscous secretion produced by and covering mucous membranes; lubricates and protects the mucous membrane and traps foreign substances.

murmur (MUR-mur) Abnormal sound produced within the heart.

muscle fiber (MUSS-el) Muscle cell.

muscle tissue One of the four major tissue types; consists of cells with the ability to contract; includes skeletal, cardiac, and smooth muscle.

muscle twitch Contraction of an entire muscle in response to a stimulus that causes an action potential in one or more muscle fibers.

muscularis (muss-kyu-LAR-is) Outermost, smooth muscle coat of a hollow organ.

muscularis mucosa Inner, thin layer of smooth muscle found in most parts of the digestive tract outside the lamina propria.

myelinated (MY-eh-lin-ay-ted) [G. *myelos,* marrow] Nerve fibers having a myelin sheath.

myelin sheath (MY-eh-lin) Lipoprotein envelope made by wrapping the cell membrane of a Schwann cell or an oligodendrocyte around an axon.

myocardium (MY-oh-KAR-dee-um) [*myo-* + G. *kordin,* heart] Middle layer of the heart, consisting of cardiac muscle.

myofibril (my-oh-FIE-brill) Fine, longitudinal fibril within a skeletal muscle fiber; consisting of sarcomeres composed of thick (myosin) and thin (actin) myofilaments, placed end to end.

myofilament (my-oh-FIL-ah-ment) Ultramicroscopic protein thread helping form myofibrils in skeletal muscle; thin myofilaments are composed of actin, and thick myofilaments are composed of myosin.

myometrium (my-oh-MEE-tree-um) Muscular wall of the uterus, composed of smooth muscle.

myosin myofilament (MY-oh-sin) One of the two major kinds of protein fibers of a sarcomere; thick filament resembling a bundle of golf clubs.

myxedema (mik-seh-DEE-mah) Hypothyroidism characterized by edema beneath the skin due to a change in the structure of the subcutaneous connective tissue.

NADH See *nicotinamide adenine dinucleotide.*

nail (neyl) Thin, horny plate at the ends of the fingers and toes, consisting of several layers of dead epithelial cells containing a hard keratin.

naris (NAH-ris), pl. **nares** (NAH-reez) Nostril, the opening into the nasal cavity.

nasal cavity (NAY-zal) Cavity divided by the nasal septum and extending from the external nares anteriorly to the nasopharynx posteriorly; bounded inferiorly by the hard palate.

nasolacrimal duct (NAY-zoh-LAK-rim-al) [L. *nasus,* nose + *lacrima,* tear] Duct that leads from the lacrimal sac to the nasal cavity.

nasopharynx (NAY-zoh-FAIR-inks) Part of the pharynx that lies above the soft palate; anteriorly, it opens into the nasal cavity.

negative feedback Mechanism by which any deviation from an ideal normal value or set point is resisted or negated; returns a

parameter to its normal range and thereby maintains homeostasis.

neonate (NEE-oh-nate) [G. *neos,* new + L. *natalis,* relating to birth] Newborn, from birth to 1 month.

neoplasm (NEE-oh-plazm) [*neo* + G. *plasma,* thing formed] New growth; an abnormal tissue that grows by cellular proliferation; may be benign or malignant.

nephron (NEF-ron) [G. *nephros,* kidney] Functional unit of the kidney, consisting of the renal corpuscle, the proximal convoluted tubule, the loop of Henle, and the distal convoluted tubule.

nerve (NERV) Collection of axons in the peripheral nervous system; conducts action potentials to and from the central nervous system.

nerve cell See *neuron*.

nerve tract Bundle of axons, their sheaths, and accompanying connective tissues located in the central nervous system.

nervous tissue (NER-vus) One of the four major tissue types; consists of neurons, which have the ability to conduct action potentials, and neuroglia, which are support cells.

neural crest cell (NYU-ral) Cell derived during embryonic development from the crests of the neural folds; gives rise to facial structures, pigment cells, and peripheral nerve ganglia.

neural tube Tube formed from the neuroectoderm in the embryo by closure of the neural groove; develops into the brain and spinal cord.

neuroectoderm (noor-oh-EK-toh-derm) Part of the ectoderm that forms the neural tube and neural crest.

neuroglia (nyu-ROH-glee-ah) [G. *neuro,* nerve + *glia,* glue] See *glial cell*.

neuromuscular junction (NYUR-oh-MUSS-kyu-lar) Synaptic junction between a nerve axon and a muscle fiber.

neuron (NYUR-on) [G., nerve] Cell capable of receiving a stimulus and propagating an action potential; a nerve cell.

neurotransmitter (NYUR-oh-trans-MIT-er) [G. *neuro,* nerve + L. *transmitto,* to send across] Chemical that is released by a presynaptic cell into the synaptic cleft and that acts on the postsynaptic cell to cause a response.

neutron (NOO-tron) [L. *neuter,* neither] Electrically neutral particle in the nucleus of atoms.

neutrophil (NEW-troh-fill) [L. *neuter,* neither + G. *phileo,* to love] White blood cell with granules that stains equally with either basic or acidic dyes; phagocytic white blood cell.

nicotinamide adenine dinucleotide (NADH) (nik-oh-TIN-a-myde AD-eh-neen dye-NOO-klee-oh-tide) Base-containing organic molecule capable of accepting hydrogen atoms and transferring energy from glycolysis and the citric acid cycle to the electron-transport chain.

nitroglycerin (ny-troh-GLIS-er-in) Glyceryl trinitrate used as a vasodilator, especiallyin angina pectoris.

nociceptor (NOH-see-sep-ter) [L. *oceo,* hurt, pain, injury + *capio,* to take] Peripheral sensory receptor or mechanism for the reception and transmission of painful or injurious stimuli.

node of Ranvier (RON-vee-ay) Unmyelinated area of an axon, every 0.1–1.0 mm, between adjacent oligodendrocytes of an axon in the central nervous system and between individual Schwann cells of the peripheral nervous system.

nonpolar molecule A molecule formed by nonpolar covalent bonds where there is equal sharing of electrons between atoms of the molecule. A nonpolar molecule carries a neutral charge.

norepinephrine (NOR-ep-ih-NEF-rin) Neurotransmitter substance released from most of the postganglionic neurons of the sympathetic division; hormone released from the adrenal cortex that increases cardiac output and blood glucose levels.

notochord (NOH-toh-kord) [G. *notor,* back + *chorde,* cord or string] Small rod of tissue lying ventral to the neural tube; characteristic of all vertebrates; in humans, it becomes the nucleus pulposus of the intervertebral disks.

nuclear pore (NOO-klee-ar) Point where the inner and outer membranes of the nuclear envelope come together to form a hole.

nuclear receptor Receptor molecule for nonpolar hormones, including thyroid and steroid hormones, found inside the target cell for these hormones. Binding of a ligand to a nuclear receptor activates synthesis of a specific protein.

nuclease (NOO-klee-ayse) Enzyme that breaks down nucleic acids.

nucleic acid (noo-KLEE-ik, KLAY-ik) Molecule consisting of many nucleotides chemically bound together; deoxyribonucleic acid and ribonucleic acid.

nucleolus (noo-KLEE-oh-lus), pl. **nucleoli** (noo-KLEE-oh-lie) Rounded, dense, well-defined nuclear body with no surrounding membrane; subunits of ribosomes are manufactured within the nucleolus.

nucleotide (NOO-klee-oh-tide) Basic building block of nucleic acids, consisting of a sugar molecule (either ribose or deoxyribose), one of several types of organic bases, and a phosphate group.

nucleus (noo-klee-us), pl. **nuclei** (noo′kle¯-ī) [L., a little nut, stone of a fruit] Cell organelle containing most of the genetic material of the cell; center of an atom consisting of protons and neutrons; collection of neuron cell bodies in the central nervous system.

nutrient (NOO-tree-ent) [L. *nutriens,* to nourish] Chemical taken into the body and used to produce energy, provide building

blocks for new molecules, or function in other chemical reactions.

nutrition (noo-TRISH-un) Process by which nutrients are obtained and used in the body.

oblique section (ob-LEEK) Cut made at other than a right angle to the long axis of an organ.

obturator (OB-tour-ate-or) [L., to occlude or stop up] Any occluding structure or a foramen so occluded, as with the obturator foramen of the hip.

occipital (ok-SIP-it-al) Back of the head.

octet rule The tendency of atoms to form bonds with other atoms through sharing or transfer of electrons until the valence shell of the bonding atoms each has 8 electrons (for hydrogen, the valence shell will have 2 electrons).

odorant (OH-dohr-ant) Substance with an odor.

olecranon (oh-LEK-rah-non) Point of the elbow.

olfaction (ol-FAK-shun) [L., to smell] Sense of smell.

olfactory (ol-FAK-toh-ree) Relating to the sense of smell.

oligodendrocyte (OL-ih-goh-DEN-droh-site) Neuroglial cell with multiple cell processes that form myelin sheaths around axons in the central nervous system.

omental bursa (oh-MEN-tal BER-sah) Pocketlike sac inside the fold of the greater omentum.

omentum (oh-MEN-tum) [L., membrane of the bowels] Fold of peritoneum extending from the stomach to another organ.

oncology (on-KOL-oh-jee) [G. *onco,* a tumor + *logos,* to study] Study of cancer and its associated problems.

oocyte (OH-oh-site) [G. *oon,* egg + *kytos,* cell] Female gamete, or sex cell; a secondary oocyte and a polar body result from the first meiotic division, which occurs prior to ovulation; a zygote and a polar body result from the second meiotic division, which

occurs following union of the sperm cell with the secondary oocyte.

oogonium (oh-oh-GOH-nee-um), pl. **oogonia** (oh-oh-GOH-nee-ah) [G. *oon,* egg + *gone,* generation] Cell that gives rise to oocytes; has a diploid number of chromosomes.

opsin Protein portion of the rhodopsin molecule; at least three different opsins are located in cone cells.

optic (OP-tik) Relating to vision.

optic disc Region in the posterior wall of the eye where the optic nerve exits the eye; the blind spot.

optic nerve Nerve that leaves the eye and exits the orbit through the optic foramen to enter the cranial vault.

oral cavity (OR-al) Mouth; the first portion of the digestive tract.

orbit (OR-bit) Seven skull bones that surround and protect the eye; eye socket.

organ (OR-gan) [G. *organon,* tool] Part of the body composed of two or more tissue types and performing one or more specific functions.

organ of Corti Named for Italian anatomist Alfonso Corti (1822–1888). See *spiral organ*.

organ system Group of organs classified as a unit because of a common function or set of functions.

organelle (OR-gah-nell) [G. *organon,* a tool + L. *-elle*, small, a little organ] Specialized part of a cell performing one or more specific functions.

organic (or-GAN-ik) Molecules that contain a carbon atom (carbon dioxide is an exception); originally defined as molecules extracted from living organisms; the original definition became obsolete when it became possible to manufacture these molecules in the laboratory.

organism (OR-gah-nizm) Any living thing considered as a whole, whether composed of one cell or many.

organogenesis (OR-gah-noh-JEN-eh-sis) Formation of organs during embryonic development.

orgasm (OR-gaz-um) [G. *orgao,* to swell, be excited] Climax of the sexual act, often associated with a pleasurable sensation.

origin (OR-ih-jin) Less movable attachment point of a muscle.

oropharynx (OR-oh-FAIR-inks) Portion of the pharynx that lies posterior to the mouth; it is continuous above with the nasopharynx and below with the laryngopharynx.

osmosis (oz-MOH-sis) [G. *osmos,* thrusting or an impulsion] Diffusion of solvent (water) through a selectively permeable membrane from a region of higher water concentration to one of lower water concentration.

osmotic pressure (os-MOT-ik) Force required to prevent the movement of water across a selectively permeable membrane.

ossification (OS-ih-fih-KAY-shun) [L. *os,* bone + *facio,* to make] Bone formation.

osteoblast (OS-tee-oh-blast) [G. *osteo,* bone] Cell that makes bone.

osteoclast (OS-tee-oh-klast) [bone eating] Cell that digests and removes bone.

osteocyte (OS-tee-oh-site) [G. *osteon,* bone + *kytos,* cell] Mature bone cell surrounded by bone matrix.

osteon (OS-tee-on) Single central canal, with its contents, and the associated lamellae and osteocytes surrounding it. Also called a haversian system.

otolith (OH-toh-lith) [G. *ous,* ear + *lithos,* stone] Small protein and calcium carbonate weight in the maculae of the vestibule.

ovary (OH-vuh-ree) One of two female reproductive glands located in the pelvic cavity; produces the oocyte, estrogen, and progesterone.

ovulation (OV-you-LAY-shun) Release of an oocyte from the mature follicle.

oxygen deficit (OK-see-jen) Amount of oxygen required to convert the lactic acid produced during anaerobic respiration to glucose and to replenish creatine phosphate stores.

oxytocin (OK-see-TOH-sin) [G., swift birth] Peptide hormone, secreted by the posterior pituitary gland, that increases uterine contraction and stimulates milk ejection from the mammary glands.

palate (PAL-uht) Roof of the oral cavity; consists of the anterior bony part, the hard palate, and the posterior soft palate that is composed mainly of skeletal muscle and connective tissue.

pancreas (PAN-kree-as) Elongated gland extending from the duodenum to the spleen; consists of a head, a body, and atail. There is an exocrine portion, which secretes digestive enzymes, which are carried by the pancreatic duct to the duodenum, and pancreatic islets, which secrete insulin and glucagon.

pancreatic duct (pan-kree-AT-ik) Duct of the pancreas; it joins the common bile duct to empty into the duodenum.

pancreatic islet (EYE-let) Cellular mass in the tissue of the pancreas; composed of different cell types that constitute the endocrine portion of the pancreas and are the source of insulin and glucagon.

papilla (pah-PILL-ah), pl. **papillae** (pah-PILL-ee) [L., nipple] Small, nipplelike process; projection of the dermis, containing blood vessels and nerves, into the epidermis; projection on the surface of the tongue.

papillary muscle (PAP-i-lar-ee) Raised area of cardiac muscle in the ventricle to which the chordae tendineae attach.

paracrine (PAYR-ah-krin) [G. *para,* alongside + *krino,* to separate] Kind of hormone function in which the effects of the hormone are restricted to the local environment.

parafollicular cell (payr-ah-fo-LIK-yoo-lar) Cell type scattered in a network of loose connective tissue between the thyroid follicles of the thyroid gland; secretes calcitonin.

paranasal sinus (PAYR-ah-NAY-zal) Air-filled cavity within certain skull bones that connects to the nasal cavity; the four sets of paranasal sinuses are the frontal, maxillary, sphenoidal, and ethmoidal.

parasympathetic (payr-ah-sim-pah-THET-ik) [G. *para,* alongside + *sympathetic*] Subdivision of the autonomic nervous system with preganglionic neurons in the brainstem and sacral part of the spinal cord; involved in involuntary functions, such as digestion, defecation, and urination.

parathyroid gland (pair-ah-THIGH-royd) One of four glandular masses embedded in the posterior surface of the thyroid gland; secretes parathyroid hormone.

parathyroid hormone (PTH) (HOR-mohn) Hormone produced by the parathyroid gland; increases bone breakdown andblood calcium levels.

parietal (pah-RYE-eh-tal) [L. *paries,* wall] Relating to the wall of any cavity; parietal serous membranes are in contact with the walls of cavities. The parietal bones form part of the skull.

parietal peritoneum (per-ih-toh-NEE-um) [L., wall] Portion of the serous membranes of the abdominal cavity lining the inner surface of the body wall.

parotid gland (pah-ROT-id) Largest of the salivary glands; one of a pair of salivary glands located anterior and inferior to each ear.

partial pressure Pressure exerted by a single gas in a mixture of gases.

partial-thickness burn Burn that damages only the epidermis (first-degree burn) or the epidermis and part of the dermis (also called a second-degree burn).

parturition (par-toor-ISH-un) [L. *parturio,* to be in labor] Childbirth; the delivery of a baby at the end of pregnancy.

pedicle (PED-ih-kle) [L. *pedicellus,* foot] Portion of a vertebra that extends from the body to the transverse process.

pelvic cavity (PEL-vic) Space completely surrounded by the pelvic bones.

pepsin (PEP-sin) [G. *pepsis,* digestion] Principal digestive enzyme produced by the stomach; digests proteins into smaller peptide chains.

peptidase (PEP-ti-days) Enzyme capable of breaking peptide chains into smaller chains and amino acids.

peptide bond (PEP-tide) Covalent chemical bond between adjacent amino acids in a polypeptide chain.

pericardial cavity (per-ih-KAR-dee-al) [G. *peri-,* around + *kardia,* the heart] Space between the visceral and parietal pericardia, filled with pericardial fluid; a cavity that surrounds the heart.

pericardial fluid Serous fluid within the pericardial cavity.

pericardium (per-ih-KAR-dee-um) [G. *pericardion,* the membrane around the heart] Membrane consisting of the epicardium and parietal pericardium (of the serous layers) and the outer fibrous pericardium; also called the pericardial sac.

perilymph (PER-i-limf) [*peri* + G. *lympha,* clear fluid] Fluid between the bony labyrinth and the membranous labyrinth of the inner ear.

perimetrium (per-ih-MEE-tree-um) Outer layer of the uterus; also called the serous layer.

perimysium (PER-i-MIS-ee-um, PER-i-MIZ-ee-um) [*peri-* + G. *mys,* muscle] Fibrous sheath enveloping each of the skeletal muscle fascicles.

perineum (PER-ih-NEE-um) Area inferior to the pelvic diaphragm between the thighs; extends from the coccyx to the pubis.

periodontal (PER-ee-oh-DON-tal) [*peri-* + G. *odous,* tooth] Referring to structures surrounding the tooth, primarily in the alveolus.

periosteum (PER-ee-OSS-tee-um) [*peri-* + G. *osteon,* bone] Thick, double-layered connective tissue sheath covering the entire surface of a bone, except the articular surface, which is covered with cartilage.

peripheral nervous system (PNS) Part of the nervous system not surrounded by the skull or vertebral column; consists of nerves and ganglia.

peripheral resistance (PR) Resistance to blood flow in all the blood vessels.

peristaltic waves (per-ih-STAL-tik) [*peri-* + G. *stalsis,* constriction] Waves of relaxation followed by waves of contraction moving along a tube; propel food along the digestive tract.

peritoneal cavity (per-ih-toh-NEE-al) [to stretch over] Space between the visceral and parietal peritoneum filled with peritoneal fluid; cavity that surrounds many abdominopelvic organs.

peritoneal membrane Serous membrane associated with the peritoneal cavity.

peritubular capillary (PER-ih-TOO-byu-lar) Capillary network in the cortex of the kidney; associated with the distal and proximal convoluted tubules.

peroxisome (per-OK-si-sohm) Membrane-bound body similar to a lysosome in appearance but often smaller and irregular in shape; contains enzymes that either decompose or synthesize hydrogen peroxide.

Peyer patch Named for Swiss anatomist Johann Peyer (1653–1712). Collection of lymphatic nodules in the distal half of the small intestine and in the appendix.

pH scale Measure of the hydrogen ion concentration of a solution; the scale extends from 0 to 14.0—a pH of 7.0 is neutral, a pH of less than 7 acidic, and a pH of greater than 7 basic.

phagocytosis (FAG-oh-sigh-TOH-sis) [G. *phagein,* to eat + L. *kytos,* cell + *osis,* condition] Ingestion and digestion by cells of

substances, such as other cells, bacteria,cell debris, and foreign particles.

pharynx (FAIR-inks) [G. *pharynx,* throat] Joint openings of the digestive tract and the windpipe. The part of the digestive and respiratory tracts superior to the larynx and esophagus and inferior and posterior to the oral and nasal cavities.

phenotype (FEE-noh-type) [G. *phaino,* to display + *typos,* model] Characteristic observed in the individual resulting from expression of the genotype.

pheromones (FAIR-oh-moans) [G. *pherē,* to carry + *hormā o,* to excite] Chemical signals secreted by an individual into the environment and perceived by a second individual of the same, or similar, species, producing a change in sexual or social behavior of that individual.

phlebitis (fleh-BIE-tis) Inflammation of a vein.

phospholipid (fos-foh-LIP-id) Lipid with phosphorus resulting in a molecule with a polar and a nonpolar end; main component of cell membranes.

photoreceptor (foh-toh-ree-SEP-tor) Sensory receptor that is sensitive to light–for example, rods and cones of the retina.

physiology (fiz-ee-OL-oh-jee) [G. *physis,* nature + *logos,* study] Scientific discipline that deals with the processes or functions of living things.

pia mater (PEE-ah MAY-ter) [L., affectionate mother] Innermost meningeal layer; tightly attached to the brain and spinal cord.

pineal gland (PIN-ee-al) [L. *pineus,* pinecone-shaped] Small endocrine gland attached to the dorsal surface of the diencephalon; may influence the onset of puberty and may play a role in some long-term cycles.

pinocytosis (PIN-oh-sigh-TOH-sis) [G. *pineo,* to drink + *kytos,* cell; *osis,* condition] Cell drinking; uptake of liquid by a cell.

pituitary dwarf (dwawrf) Individual of short stature, of relatively normal proportion, as a result of insufficient growth hormone secreted from the anterior pituitary gland.

pituitary gland (pih-TOO-ih-tair-ee) [L. *pituita,* phlegm or a thick mucous secretion] Endocrine gland attached to the hypothalamus by the infundibulum; secretes hormones that influence the function of several other glands and tissues.

placenta (plah-SEN-tah) Structure derived from embryonic and maternal tissues by which the embryo and fetus are attached to the uterus.

plasma (PLAZ-mah) Fluid portion of blood; blood minus the formed elements.

plasma cell Cell derived from B cells; produces antibodies.

plasma membrane See *cell membrane.*

plasmin (PLAZ-min) Enzyme that breaks down the fibrin in blood clots; derived from plasminogen.

plateau phase Prolongation of the depolarization phase of a cardiac muscle cell membrane; results in a prolonged refractory period.

platelet (PLAYT-let) Minute fragment of cells derived from megakaryocytes; plays an important role in preventing blood loss.

platelet plug Accumulation of platelets that stick to connective tissue and to one another and prevent blood loss from damaged blood vessels.

pleural (PLUR-al) [G., a rib or cavity] **cavity** Space between the visceral and parietal pleura, filled with pleural fluid; a cavity that surrounds each lung.

pleural membrane Serous membrane associated with the lungs.

plexus (PLEK-sus) [L., a braid] Intertwining of nerves or blood vessels.

PMS See *premenstrual syndrome.*

pneumothorax (new-moh-THOR-aks) Presence of air in the pleural cavity.

podocyte (POD-oh-syte) [Fr. *pous, podos,* foot + G. *kytos,* a hollow (cell)] Epithelial cell of Bowman's capsule attached to the outer surface of the glomerular capillary basement membrane; forms part of the filtration membrane.

polar body Oocyte receiving little cytoplasm; results from the first and the second meiotic division.

polar covalent bond Chemical bond in which electrons are shared unequally between two atoms.

polar molecule A molecule formed by polar covalent bonds or ionic bonds where there is an unequal sharing or a transfer of electrons between atoms of the molecule. A polar molecule carries a charge.

polarize To create a difference in potential (charge) between two points, as between the inside and outside of a cell membrane.

polycythemia (POL-ee-sigh-THEE-me-ah) [G. *polys,* many + *kytos,* cell] Increase in red blood cell numbers above the normal value.

polypeptide A chain of covalently bonded amino acids that forms a part of, or the entirety of, a protein molecule.

polysaccharide (pol-ee-SACK-ah-ride) [many sugars] Many monosaccharides chemically bound together, such as glycogen and starch.

pons (PONZ) [L., bridge] Part of the brainstem between the medulla oblongata and midbrain; contains nerve tracts between the cerebrum and cerebellum, as well as ascending and descending tracts.

portal system (POR-tal) System of vessels in which blood, after passing through one capillary bed, is conveyed through a second capillary network.

positive feedback Mechanism by which any deviation from an ideal normal value or set point is made greater.

posterior (pos-TEER-ee-or) [L. *posterus,* following] That which follows; in humans, toward the back.

posterior pituitary gland Posterior portion of the pituitary gland, which consists of processes of nerve cells that have their cell bodies located in the hypothalamus; secretes oxytocin and antidiuretic hormone.

postganglionic (POST-gang-glee-ON-ik) Autonomic neurons whose cell bodies are located outside the central nervous system and that receive synaptic stimulation from preganglionic autonomic neurons.

preganglionic (PREE-gang-glee-ON-ik) Autonomic neurons whose cell bodies are located in the central nervous system and that synapse with postganglionic neurons.

preload (PREE-lohd) Degree to which the ventricular wall is stretched at the end of diastole; increases as the venous return increases.

premenstrual syndrome (PMS) (PREE-MEN-stroo-al SIN-drohm) In some women of reproductive age, the regular monthly experience of physiological and emotional distress, usually during the few days preceding menses, typically involving fatigue, edema, irritability, tension, anxiety, and depression.

prenatal period (pree-NAY-tal) [L. *prae,* before + *natalis,* relating to birth] Period before birth.

prepuce (PREE-puce) In the male, a free fold of skin that almost completely covers the glans penis; the foreskin; in the female, a fold of mucous membrane that covers the clitoris.

primary response Immune response that occurs as a result of the first exposure to an antigen; results in the production of antibodies and memory cells.

prime mover Muscle that plays the principal role in accomplishing a movement.

primitive streak Shallow groove in the ectodermal surface of the embryonic disk; cells migrating through the streak become mesoderm.

process (PROS-es, PROH-ses) Projection on a bone.

product (PROD-uhkt) Substance produced in a chemical reaction.

progesterone (proh-JESS-ter-ohn) Hormone secreted primarily by the corpus luteum and the placenta; aids in growth and development of female reproductive organs and secondary sexual characteristics; causes growth and maturation of the endometrium of the uterus during the menstrual cycle.

prolactin (proh-LAK-tin) [L. *pro,* precursor + *lact,* milk] Hormone of the anterior pituitary gland that stimulates the secretion of milk.

pronation (proh-NAY-shun) [L. *pronare,* to bend forward] Rotation, as of the forearm, starting in the anatomical position, so that the anterior surface faces posteriorly.

prophase (PROH-fayz) [G. *prophasis,* to foreshadow] First stage of mitosis or meiosis, consisting of contraction and increase in thickness of the chromosomes.

prostaglandin (PROS-tah-GLAN-din) Class of physiologically active substances present in many tissues; effects include vasodilation, stimulation and contraction of uterine smooth muscle, and promotion of inflammation and pain.

prostate gland (PROS-tate) [G. *prostates,* one standing before] Gland that surrounds the beginning of the urethra in the male. The secretion of the gland is a milky fluid that is discharged into the urethra as part of the semen.

protein (PRO-teen) [G. *proteios,* primary] Large molecule consisting of long sequences of amino acids (polypeptides) linked by peptide bonds.

proteoglycan (PROH-tee-oh-GLYE-kan) [G. *proteo,* protein + *glycan,* polysaccharide] Macromolecule consisting of numerous polysaccharides attached to a common protein core; attracts and retains large amounts of water.

proteolytic (PROH-tee-oh-LIT-ik) Enzyme capable of digesting proteins or polypeptides.

proton (PROH-ton) [G. *protos,* first] Positively charged particle in the nuclei of atoms.

provitamin (proh-VITE-ah-min) Substance that can be converted into a vitamin.

proximal (PROK-sih-mal) [L. *proximus,* nearest] Closer to the point of attachment to the body than another structure.

proximal convoluted tubule Convoluted portion of the nephron that extends from Bowman's capsule to the descending limb of the loop of Henle.

PTH See *parathyroid hormone.*

puberty (PYU-ber-tee) [L. *pubertas,* grown up] Series of events that transform a child into a sexually mature adult; involves an increase in the secretion of all reproductive hormones.

pudendal cleft (pu-DEN-dal) [L. *pudeo,* to feel ashamed] Cleft between the labia majora.

pudendum (pu-DEN-dum), pl. **pudenda** (pu-DEN-da) External genitals, especially the female genitals. See *vulva.*

pulmonary capacity (PULL-moh-NAIR-ee) Sum of two or more pulmonary volumes.

pulmonary circulation Blood flow through the system of blood vessels that carry blood from the right ventricle of the heart to the lungs and back from the lungs to the left atrium.

pulmonary semilunar valve Semilunar valve at the base of the pulmonary trunk where it exits from the right ventricle.

pulmonary trunk Large, elastic artery that carries blood from the right ventricle of the heart to the right and left pulmonary

arteries.

pulmonary volume Lung volume, measured by spirometry; deviations from a normal value can be used to diagnose certain lung diseases; the pulmonary volumes are the tidal volume, inspiratory reserve volume, expiratory reserve volume, and residual volume.

pulp (PULP) [L. *pulpa,* flesh] Soft tissue inside a tooth, consisting of connective tissue, blood vessels, nerves, and lymphatic vessels.

pulse (puhls) Pressure wave that travels rapidly along the arteries when blood is ejected from the left ventricle into the aorta.

pulse pressure Difference between systolic and diastolic pressures.

pupil (PYU-pill) [L. *pupa,* a doll, so called because you can see a little reflection, or doll, in the pupil of another person's eye] Opening in the iris of the eye through which light enters.

Purkinje fiber (per-KIN-jee) Named for Bohemian anatomist/physiologist Johannes Purkinje (1787–1869). A specialized cardiac muscle fiber that conducts action potentials through cardiac muscle; forms part of the conduction system of the heart.

pus (puhs) Product of inflammation, consisting of a liquid containing white blood cells, dead cells, and cell fragments.

pyloric sphincter (pie-LOR-ik) [G., gatekeeper] Thickened ring of smooth muscle at the distal end of the stomach.

pyrogen (PYE-roh-jen) Chemical released by microorganisms, neutrophils, monocytes, and other cells that stimulates fever production by acting on the hypothalamus.

pyruvic acid (pye-ROO-vik) Three-carbon end product of glycolysis; two pyruvic acid molecules are produced from each glucose molecule.

quadrant (KWAD-rant) [L. *quadrans,* a quarter] One-quarter of a circle; the abdomen is divided into right upper, right lower, left

upper, and left lower quadrants by a horizontal and a vertical line intersecting at the umbilicus.

reactant (ree-AK-tant) Substance taking part in a chemical reaction.

receptor (ree-SEP-tor) [L., receiver] Protein molecule on the cell surface or within the cytoplasm that binds to a specific factor, such as a drug, a hormone, an antigen, or a neurotransmitter; one of the sensory nerve endings in the skin, deep tissues, viscera, and special sense organs.

recessive (ree-SES-iv) In genetics, a gene that may not be expressed phenotypically because of the expression of a contrasting dominant gene.

Recommended Daily Intake (RDI) Generally, the highest RDA value in each of four categories: infants, toddlers, people over 4 years of age, and pregnant or lactating women. The RDIs used to determine the Daily Values are based on the 1968 RDAs.

Recommended Dietary Allowances (RDAs) Guide for estimating the nutritional needs of groups of people based on their age, sex, and other factors; first established in 1941.

rectum (RECK-tum) [L. *rectus,* straight] Last, straight part of the large intestine; between the colon and the anal canal.

rectus (REK-tuhs) Straight.

red blood cell (RBC) Biconcave disk that contains hemoglobin, which transports oxygen and carbon dioxide; red blood cells do not have a nucleus.

reflex (REE-fleks) Automatic response to a stimulius; does not require conscious thought.

reflex arc Consists of a sensory receptor, an afferent (sensory) neuron, an association neuron, an efferent (motor) neuron, and an effector organ.

regeneration (ree-JEN-eh-RAY-shun) Tissue repair in which the damaged cells are replaced by cells of the same type as those damaged.

releasing hormone Hormone that is released from neurons in the hypothalamus and flows through the hypothalamic-pituitary portal system to the anterior pituitary gland; regulates the secretion of hormones from the cells of the anterior pituitary gland.

renal capsule (REE-nal) Connective tissue capsule that surrounds each kidney.

renal corpuscle (KOR-pus-ul) Structure composed of a Bowman's capsule and its glomerulus.

renal pyramid (PIR-ah-mid) Cone-shaped structure that extends from the renal sinus, where the apex is located, into the cortex of the kidney, where the base is located.

renal sinus (SIGH-nus) Cavity central to the medulla of the kidney that is filled with adipose tissue and contains the renal pelvis.

renin (REE-nin) Enzyme secreted by the kidney that converts the plasma protein angiotensinogen to angiotensin I.

replacement Tissue repair in which the damaged cells are replaced by cells of a type different from those damaged.

respiration (RES-pih-RAY-shun) [L. *respiratio,* to breathe] Process in which oxygen is used to oxidize organic fuel molecules, providing a source of energy as well as carbon dioxide and water; includes ventilation, gas exchange, transport of oxygen and carbon dioxide in the blood, gas exchange between the blood and the tissues, and cell metabolism.

respiratory membrane (RES-pir-ah-TOR-ee) Membrane in the lungs across which gas exchange occurs with blood; consists of a thin layer of fluid, the alveolar epithelium, a basement membrane of the alveolar epithelium, interstitial space, the basement membrane of the capillary endothelium, and the capillary endothelium.

resting membrane potential Charge difference across the membrane of a resting cell (i.e., a cell that has not been stimulated to produce an action potential).

rete testis (REE-teh) Network of canals at the termination of the straight portion of the seminiferous tubules.

reticular formation (reh-TIK-you-lar) [L. *rete,* net] Loose network of neuron cell bodies scattered throughout the brainstem; involved in the regulation of cycles such as the sleep-wake cycle.

retina (RET-ih-nah) [L. *rete,* a net] Inner, light-sensitive tunic of the eye; nervous tunic.

retinaculum (ret-ih-NAK-you-lum) [L., band, bracelet, halter, to hold back] Dense regular connective tissue sheath holding down the tendons at the wrist, ankle, or other sites.

retinal (RET-ih-nal) Relating to the retina; retinaldehyde most commonly referring to the all-*trans* form (all-*trans*-retinal).

retroperitoneal (RE-troh-PER-i-toh-NEE-uhl) Located behind the parietal peritoneum; includes the kidneys, the adrenal glands, the pancreas, portions of the intestines, and the urinary bladder.

reversible reaction (ree-VER-si-bul) Chemical reaction in which the reaction can proceed from reactants to products or from products to reactants; the amount of reactants relative to products is constant at equilibrium.

rhodopsin (roh-DOP-sin) [G. *rhodon,* rose or red color + *opsin,* protein portion of rhodopsin] Purplish red protein in the external segment of the rods of the retina. Action of light converts it to opsin and all-*trans*-retinal.

ribonucleic acid (RYE-boh-noo-KLEE-ik) **(RNA)** Type of nucleic acid containing the sugar ribose; involved in protein synthesis.

ribosomal RNA (rRNA) (RYE-boh-sohm-al) RNA that is associated with certain proteins to form ribosomes.

ribosome (RYE-bo-sohm) [ribose, a specific sugar] Small, spherical, cytoplasmic organelle where protein synthesis occurs.

RNA See *ribonucleic acid*.

rod Photoreceptor cell in the retina of the eye with a rod-shaped photoreceptive process; very light-sensitive cell that is important in dim light.

rotator cuff (roh-TAY-tor) Four deep muscles that attach the humerus to the scapula.

rRNA See *ribosomal RNA*.

ruga (ROO-gah) Ridge or fold in the mucous membrane of the stomach.

SA See *sinoatrial*.

sagittal plane (SAJ-ih-tal) [L. *sagitta,* the flight of an arrow] Plane running vertically through the body and dividing it into right and left parts.

saliva (sa-LIE-vah) Fluid containing enzymes and mucus; produced by the salivary glands and released into the oral cavity.

salivary gland (SAL-ih-var-ee) Gland opening into the mouth and producing saliva.

salt Molecule consisting of a positively charged ion other than hydrogen and a negatively charged ion other than hydroxide.

sarcolemma (SAR-koh-LEM-ah) [G. *sarx,* flesh, muscle; *lemma,* husk] Cell membrane of a muscle fiber.

sarcomere (SAR-koh-meer) [*sarco-* + G. *meros,* part] Part of a myofibril formed of actin and myosin myofilaments, extending from Z disk to Z disk; the structural and functional unit of a muscle.

sarcoplasm (SAR-koh-plazm) [*sarco-* + *plasma,* a thing formed] Cytoplasm of a muscle fiber.

sarcoplasmic reticulum (SAR-koh-PLAZ-mik re-TIK-you-lum) Endoplasmic reticulum of a muscle fiber.

Schwann cell Named for German histologist/physiologist Theodor Schwann (1810–1882). Neuroglial cell forming myelin sheaths

around axons in the peripheral nervous system.

sciatic (sigh-AT-ik) [Fr. *ischion,* the hip joint] Ischiadic or sciatic nerve.

sclera (SKLAIR-ah) [L. *skleros,* hard] Dense, white, opaque posterior four-fifths of the fibrous tunic of the eye; white of the eye.

scoliosis (skoh-lee-OH-sis) [G., a crookedness] Abnormal lateral curvature of the spine.

scrotum (SKROH-tum) Musculocutaneous sac containing the testes.

sebaceous gland (se-BAY-shus) [L. *sebum,* tallow] Gland of the skin that produces sebum; usually associated with a hair follicle.

sebum (SEE-bum) [L., tallow] Oily, white, fatty substance produced by the sebaceous glands; lubricates hair and the surface of the skin.

second messenger Molecule produced within a cell that binds to a macromolecule, such as receptors or enzymes inside that cell, that regulates their activities.

secondary response Occurs when the immune system is exposed to an antigen against which has already produced a primary response; involves memory cells; also called memory response.

secretin (se-KREE-tin) Hormone released from the epithelium of the duodenum; inhibits gastric secretion.

secretion (se-KREE-shun) Substance produced inside a cell and released from the cell.

selectively permeable Characteristic of the cell membrane that allows some substances to cross the membrane but not others; permeability is determined by chemical characteristics such as polarity and size.

sella turcica (SEL-ah TUR-sih-kah) [L., saddle, Turkish] Saddle-shaped depression in the inner surface of the skull where the pituitary gland is located.

semen (SEE-men) [L., seed] Penile ejaculate; thick, yellowish-white, viscous fluid containing sperm cells and secretions of the testes, seminal vesicles, prostate gland, and bulbourethral glands.

semicircular canal (SEM-ee-SIR-kyoo-lar) One of three canals in each temporal bone; involved in the detection of motion.

semilunar valve (sem-ee-LOO-nar) One of two valves in the heart composed of three crescent-shaped cusps that prevent blood flow into the ventricles following ejection; located at the beginning of the aorta and pulmonary trunk.

seminal vesicle (SEM-in-al VES-ih-kull) One of two glandular structures that empty into the ejaculatory ducts; its secretion is one of the components of semen.

seminiferous tubule (sem-ih-NIF-er-us) Tubule in the testis in which sperm cells develop.

sensory neuron Neuron that extends from sensory receptors in the periphery to the central nervous system.

septum (SEP-tum) [L. *saeptum,* a partition or wall] Thin wall dividing two cavities or masses of softer tissue.

serosa (seh-ROH-sa) Smooth, outermost covering of an organ where it faces a cavity and is not surrounded by connective tissue.

serous membrane (SEER-us) Thin sheet consisting of epithelium and connective tissue that lines cavities not opening to the outside of the body; does not contain glands but does secrete serous fluid.

serum (SEER-um) Fluid portion of blood after the removal of fibrin and formed elements.

sex chromosome Chromosome other than an autosome; responsible for sex determination.

sinoatrial (SA) node (sigh-noh-AY-tree-al) Mass of specialized cardiac muscle fibers in the right atrium near the opening of the

superior vena cava that acts as the "pacemaker" of the cardiac conduction system.

sliding filament model Mechanism by which actin and myosin myofilaments slide over one another during muscle contraction.

solute (SOL-yout, SOH-loot) [L. *solutus,* dissolved] Dissolved substance in a solution.

solution (soh-LOO-shun) Homogeneous mixture formed when a solute dissolves in a solvent (liquid).

solvent (SOL-vent) [L. *solvens,* dissolve] Liquid that holds another substance in solution.

somatic motor (soh-MAT-ik) [G. *soma,* body or bodily] Type of motor (efferent) neuron of the peripheral nervous system that innervates skeletal muscle.

specificity Antibodies and receptors work effectively only on particular antigens or ligands.

spermatid (SPER-mah-tid) Cell in the late stage of the development of the sperm cell (male gamete). It is haploid and is derived from the secondary spermatocyte.

spermatocyte (SPER-mah-TOH-syte) Cell arising from a spermatogonium and destined to give rise to spermatozoa.

spermatogenesis (SPER-mat-oh-JEN-eh-sis) Formation and development of sperm cells.

spermatogonium (SPER-mah-toh-GOH-nee-um), pl. **spermatogonia** (SPER-mah-toh-GOH-nee-ah) Most peripheral germ cell in the seminiferous tubules scattered between the sustentacular cells; divide by mitosis and some form primary spermatocytes.

spermatozoon (SPER-mah-toh-ZOH-on), pl. **spermatozoa** (SPER-mat-oh-ZOH-ah) [G. *sperma,* seed + *zoon,* animal] Male gamete, or sex cell, composed of a head, midpiece, and tail;

contains the genetic information transmitted by the male; sperm cell.

sperm cell [G. *sperma,* seed] Male reproductive cell; see also *spermatozoon.*

sphenoid (SFEE-noyd) [G. *sphenoeides,* wedge + *eidos,* resemblance] Sphenoid bone or relating to the sphenoid bone.

sphygmomanometer (SFIG-moh-mah-NOM-ih-ter) [G. *sphygmos,* pulse; *manos* + *metron,* measure] Instrument for measuring blood pressure consisting of an arm sleeve and an inflating bulb with a device attached for measuring pressure in the arm sleeve.

spina bifida (SPY-nah BIH-fih-dah) Defect in the spinal column, consisting in absence of the vertebral arches, through which the spinal membranes, with or without spinal cord tissue, may protrude.

spinal cord Portion of the central nervous system extending from the foramen magnum at the base of the skull to the second lumbar vertebra; consists of a central gray portion and a peripheral white portion.

spinal nerve Peripheral nerve exiting from the spinal cord.

spirometer (spy-ROM-eh-ter) [L. *spiro,* to breathe + G. *metron,* measure] Meter used for measuring the volume of respiratory gases; usually consists of a counterbalanced, cylindrical bell sealed by dipping into a circular trough of water.

spirometry (spy-ROM-eh-tree) Process of making pulmonary measurements with a spirometer.

spleen (SPLEEN) Large lymphatic organ in the left upper part of the abdominal cavity, between the stomach and the diaphragm; composed of white and red pulp; responds to foreign substances in the blood, destroys worn-out red blood cells, and is a reservoir for blood.

spongy bone [L., grating or lattice] Bone with a latticelike appearance.

squamous (SKWAY-mus) [L. *squama,* a scale] Scalelike, flat.

stapes (STAY-pees) [L., stirrup] The third of the three middle ear bones; attached to the oval window; the stirrup.

Starling's law of the heart Named for English physiologist Ernest Starling (1866–1927). Force of contraction of cardiac muscle is a function of the length of its muscle fibers at the end of diastole; the greater the degree of filling of the heart (the greater the venous return), the greater the force of contraction of the cardiac muscle.

stem cell Single population of cells that differentiate to give rise to the formed elements of blood.

stenosed valve (STEN-ohzd) Valve that has its opening narrowed or partially closed.

steroid (STER-oyd) Large family of lipids, including some hormones, vitamins, and cholesterol.

stethoscope (STETH-oh-skope) [G. *stetho-,* chest + *skopeo,* to view] Instrument originally devised for aid in hearing the respiratory and cardiac sounds in the chest and now used in hearing other sounds in the body as well.

stimulus An object or event that provokes a particular response by an organ or a tissue.

stratum (STRAH-tum), pl. **strata** (STRAH-tah) [L., bed cover, layer] Layer of tissue.

stratum basale (ba-SAL-eh) Deepest layer of the epidermis; consists of columnar cells that undergo mitotic divisions.

stratum corneum (COR-nee-um) Most superficial layer of the epidermis; consists of dead squamous cornified cells that have undergone keratinization.

stria, pl., striae (STRI-ae) [L., channel, furrow] Bands of thin, wrinkled skin, becoming red and white, that occur commonly on the abdomen, buttocks, and thighs at puberty and/or during and following pregnancy and result from overextension of the skin.

stroke volume Volume of blood ejected from either the right or the left ventricle during each heartbeat.

styloid (STY-loyd) [G. *stylos,* a stake or pen] Slender, pencil-shaped process.

subarachnoid space (sub-ah-RAK-noyd) Fluid-filled space below the arachnoid layer covering the brain and spinal cord; contains cerebrospinal fluid.

subcutaneous (sub-kew-TAY-nee-us) [L. *sub,* under + *cutis,* skin] **tissue** Under the skin; same tissue as the hypodermis.

sublingual gland (sub-LING-wal) One of a pair of salivary glands located below the tongue.

submandibular gland (sub-man-DIB-you-lar) One of a pair of salivary glands located below the mandible.

submucosa (sub-mew-KOH-sa) Layer of connective tissue deep to the mucous membrane.

sulcus (SUL-cuss), pl. **sulci** (SUL-sigh) [L., ditch] Groove on the surface of the brain between gyri.

superficial (soo-per-FISH-al) [L. *superficialis,* surface] Toward or on the surface.

superior (soo-PEE-ree-or) [L., higher] Up, or higher, with reference to the anatomical position.

superior vena cava (VEE-nah KAY-vah) Blood vessel that receives blood from the head, neck, and upper limbs and empties into the right atrium of the heart.

supination (soo-pih-NAY-shun) [L. *supino,* to place something on its back] Rotation of the forearm so that the anterior surface is anterior; that is, the forearm is in the anatomical position.

surfactant (ser-FAK-tant) Mixture of lipoprotein molecules produced by the secretory cells of the alveolar epithelium of the lung; reduces water surface tension.

sustentacular cell (sus-ten-TAK-you-lar) Cell in the wall of the seminiferous tubules to which spermatogonia and spermatids

are attached; also called a Sertoli cell.

suture (SOO-chur) [L. *surtura,* a seam] Fibrous joint between flat bones of the skull.

sweat gland (swet) Usually, a secretory organ that produces a watery secretion, called sweat, that is released onto the surface of the skin; some sweat glands, however, produce an organic secretion.

sympathetic (sim-pah-THET-ik) [G. *sympatheo,* to feel with + *pathos,* suffering] Subdivision of the autonomic nervous system with preganglionic nerve cell bodies located in the thoracic and lumbar regions of the spinal cord; generally involved in preparing the body for immediate physical activity.

synapse (SIN-aps) [G. *syn,* together + *haptein,* to clasp] Junction between a nerve cell and another nerve cell, muscle cell, or gland cell; in a chemical synapse, chemicals are released from the nerve cell as a result of an action potential in the nerve cell, the chemicals cross the cleft between the cells, and they cause a response in the postsynaptic cell.

synapsis (si-NAP-sis) Pairing of homologous chromosomes during prophase of the first meiotic division.

synergist (SIN-er-jist) Muscle that works with another muscle to cause a movement.

synovial cavity (sih-NOH-vee-al) [G. *syn,* coming together + *ovia,* resembling egg albumin] Cavity surrounding articulating bones of a freely movable or synovial joint; contains synovial fluid.

synovial fluid Somewhat viscous substance serving as a lubricant in movable joints, tendon sheaths, and bursae.

synovial joint Freely movable joint.

synovial membrane Membrane that lines the inside of a joint cavity; produces synovial fluid.

synthesis reaction (SIN-the-sis) Combination of atoms, ions, or molecules to form a new, larger molecule.

systemic circulation (sis-TEM-ik) Blood flow through the system of blood vessels that carry blood from the left ventricle of the heart to the tissues of the body and back from the body to the right atrium.

systemic inflammation Inflammation that occurs in many areas of the body; in addition to the symptoms of local inflammation, can include increased neutrophil numbers in the blood, fever, and shock.

systole (SIS-toh-lee) [G., a contracting] Contraction of the heart chambers, during which blood leaves the chambers; usually refers to ventricular contraction.

systolic pressure (sis-TOL-ik) Maximum arterial blood pressure reached during ventricular systole.

target tissue Tissue on which a hormone acts.

taste bud Sensory structure mostly on the tongue; functions as a taste receptor.

tectorial membrane (tek-TOR-ee-al) [L., a covering] Membrane attached to the spiral lamina and extending over the hair cells; hairs of the hair cells have their tips embedded in the membrane.

telophase (TEL-oh-fayz) [G. *telos,* end + *phasis,* an appearance] Final stage of mitosis or meiosis that begins when migration of chromosomes to the poles of the cells has been completed.

temporal (TEM-por-al) [L. *tempus,* time] Indicating the temple; the temple of the head is so named because it is there that the hair first begins turning white, indicating the passage of time.

tendinous intersection (TEN-di-nuhs) One of the bands of connective tissue crossing the rectus abdominis muscle, subdividing it and attaching it to adjacent connective tissue.

tendon (TEN-dun) Tough connective tissue band connecting a muscle to bone.

teniae coli (TEE-nee-aye KOH-lye) [G. *tainia,* band, tapeworm + *coli,* colon] Segmented, longitudinal smooth muscle layer of the colon.

testis (TES-tis), pl. **testes** (TES-teez) One of two male reproductive glands in the scrotum; produces testosterone and sperm cells.

testosterone (tes-TOSS-ter-ohn) Steroid hormone secreted primarily by the testes; aids in spermatogenesis, controls maintenance and development of male reproductive organs and secondary sexual characteristics, and influences sexual behavior.

tetanus (TET-ah-nuss) [L. *tetanus,* convulsive tension] Sustained muscular contraction caused by a series of nerve stimuli repeated so rapidly that the individual contractions are fused, producing a sustained tetanic contraction; also a disease marked by painful tonic muscular contractions, caused by the neurotoxin of *Clostridium tetani* action on the central nervous system.

tetany (TET-ah-nee) Condition in muscle contraction in which there is no relaxation between muscle twitches.

tetraiodothyronine (TET-rah-eye-oh-doh-THY-roh-neen) **(T_4)** One of the thyroid hormones; contains four iodine atoms; also called thyroxine.

thalamus (THAL-ah-mus) [G., a bedroom] Large mass of gray matter making up the bulk of the diencephalon; involved in the relay of sensory input to the cerebrum.

thoracic cavity (thor-ASS-ik) Space bounded by the neck, the thoracic wall, and the diaphragm.

thoracic duct Largest lymphatic vessel in the body; drains the left side of the head and neck, the left upper thorax, the left upper limb, and the inferior half of the body into the left subclavian vein.

thorax (THOR-acks) [G., breastplate] Chest; the upper part of the trunk between the neck and the abdomen.

threshold Value of the membrane potential at which an action potential is produced as a result of depolarization in response to a stimulus.

thrombocyte (THROM-boh-site) [*thrombos-*, clot + G. *kytos,* cell] See *platelet*.

thrombosis (throm-BOH-sis) [G. *thrombos,* clot] Formation or presence of a clot (thrombus) inside a blood vessel.

thrombus (THROM-bus) [G. *thrombos,* clot] Clot within the cardiovascular system.

thymosin (THIGH-moh-sin) Hormone secreted from the thymus that helps activate the immune system.

thymus (THIGH-mus) [G. *thymos,* sweetbread] Bilobed lymphatic organ located in the inferior neck and superior mediastinum; involved with the maturation of T cells.

thyroid cartilage (THIGH-royd) [G. *thyreoeides,* shield] Largest laryngeal cartilage; forms the laryngeal prominence, or Adam's apple.

thyroid follicle One of many small spheres with walls consisting of cuboidal epithelial cells in the thyroid gland; filled with proteins to which thyroid hormones are attached until they are secreted.

thyroid gland Endocrine gland located inferior to the larynx and consisting of two lobes connected by a narrow band; secretes the thyroid hormones.

thyroid hormone Any hormone secreted by the thyroid gland, especially those, such as thyroxine, that contain iodine and regulate metabolism and the maturation of tissues.

thyroid-stimulating hormone (TSH) Hormone released from the hypothalamus that stimulates thyroid hormone secretion from the thyroid gland.

thyroxine (thigh-ROK-seen) See *tetraiodothyronine*.

tissue (TISH-you) [L. *texo,* to weave] Collection of cells with similar structure and function and the substances between the cells.

tissue repair Substitution of viable cells for damaged or dead cells by regeneration or replacement.

tonsil (TON-sill) Collection of lymphoid tissue; usually refers to large collections of lymphoid tissue beneath mucous membranes of the oral cavity and pharynx; lingual, pharyngeal, and palatine tonsils.

trabecula (trah-BEK-yoo-lah) [L. *trabs,* beam] Beam or plate of spongy bone or other tissue.

trachea (TRAY-kee-ah) [G. *tracheia arteria,* rough artery] Air tube extending from the larynx into the thorax, where it divides to form bronchi; has 16–20 C-shaped pieces of cartilage in its walls.

tracheostomy (tray-kee-OST-oh-mee) Incision into the trachea.

tract (TRAKT) Nerve tract; a bundle of neuron cell processes (axons) in the central nervous system, usually having a common function.

transfer RNA (tRNA) RNA that attaches to individual amino acids and transports them to the ribosomes, where they are connected to form a protein polypeptide chain.

transfusion Transfer of blood from one person to another.

transverse plane (trans-VERS) Plane separating the body into superior and inferior parts.

transverse section Cut made at right angles to the long axis of an organ.

triacylglycerol (try-AS-il-GLISS-er-ol) See *triglyceride.*

tricuspid valve (try-KUSS-pid) Valve closing the opening between the right atrium and right ventricle of the heart.

triglyceride (trie-GLISS-eh-ride) Common type of lipid, or fat, with three fatty acids bound to a glycerol molecule; also called a triacylglycerol.

trigone (TRY-gohn) [L. *trigonium,* triangle] Triangular, smooth area at the base of the urinary bladder between the openings of the two ureters and that of the urethra.

triiodothyronine (trie-EYE-oh-doh-THIE-roh-neen) **(T_3)** One of the thyroid hormones; contains three iodine atoms.

tRNA See *transfer RNA.*

trochanter (TROH-kan-ter) [G., a runner] One of the large tubercles of the proximal femur.

tropic hormone A hormone that stimulates the secretion of another hormone. Many tropic hormones are secreted by the anterior pituitary.

trophoblast (TROH-foh-blast) [G. *trophe,* nourishment + *blastos,* germ] Outer part of the blastocyst; enters the uterus and becomes the embryonic portion of the placenta.

trypsin (TRIP-sin) Enzyme released from the pancreas that digests proteins.

TSH See *thyroid-stimulating hormone.*

tubercle (TOO-ber-kul) Lump or knob on a bone.

tuberosity (TOO-ber-OS-i-tee) Lump on a bone, usually larger than a tubercle.

tubular reabsorption Movement of materials, by means of diffusion or active transport, from the filtrate within a nephron into the blood.

tubular secretion Movement of materials, by means of active transport, from the blood into the filtrate of a nephron.

tumor (TOO-mer) Swelling, one of the cardinal signs of inflammation, or a new growth of tissue in which the multiplication of cells is uncontrolled and progressive; see also *neoplasm*.

tunic (TOO-nik) [L., coat] Layer or coat; one of the three enveloping layers of the wall of the eye; the three tunics are the fibrous, vascular, and nervous tunics; one of the three layers of blood vessels: tunica intima, tunica media, and tunica adventitia.

tunica adventitia (TOO-ni-kah ad-ven-TISH-ah) Outermost fibrous coat of a vessel or an organ that is derived from the surrounding connective tissue.

tunica intima (TOO-nih-kah) Innermost layer of a blood or lymphatic vessel; consists of endothelium and a small amount of connective tissue.

tunica media Middle, usually muscular, coat of an artery or another tubular structure.

tympanic membrane (tim-PAN-ik) [drumlike] Cellular membrane that covers the inner opening of the external auditory canal and separates the middle and external ears; vibrates in response to sound waves; the eardrum.

ulcer (ULL-cer) [L. *ulcus,* a sore] Lesion on the surface of the skin or a mucous membrane, such as in the stomach or intestine, caused by a superficial loss of tissue, usually with inflammation.

umbilical cord (um-BIL-ih-kal) [L., navel] Cord connecting the fetus to the placenta; contains two umbilical arteries, which originate from the embryo's internal iliac arteries, that carry blood from the embryo to the placenta, and one umbilical vein, that carries blood back to the fetus.

umbilical vein Vein in the umbilical cord of the fetus by which the fetus receives nourishment from the placenta; becomesthe round ligament of the liver in the adult.

ureter (you-REET-er) [G. *oureter,* urinary canal] Tube conducting urine from the kidney to the urinary bladder.

urethra (you-REE-thra) Duct leading from the urinary bladder, discharging the urine externally.

uterus (YOU-ter-us) Hollow muscular organ in which the fertilized oocyte develops into a fetus.

utricle (YOU-tri-kul) Larger of the two membranous sacs in the vestibule of the labyrinth. The semicircular canals arise from it.

uvula (YOU-vyu-lah) [L. *uva,* grape] Small, grapelike appendage at the posterior margin of the soft palate.

vaccination (vak-sih-NAY-shun) Deliberate introduction of an antigen into a subject to stimulate the immune system and produce immunity to the antigen.

vaccine (vak-SEEN) Preparation of killed microorganisms, altered microorganisms, or derivatives of microorganisms intended to produce immunity; usually administered by injection, but sometimes ingestion is preferred.

vagina (vah-JIE-nah) [L., sheath] Genital canal in the female, extending from the uterus to the vulva.

valence shell The outermost shell of an atom. The electrons housed here determine the chemical reactivity of the atom.

variable region Part of an antibody that combines with an antigen; responsible for the specificity of the antibody.

varicose (VAIR-ih-kos) **vein** Vein that is so dilated that the cusps of the valves are no longer capable of preventing backflow of blood; usually the veins in the lower legs or the hemorrhoidal veins.

vasoconstriction (VAY-soh-con-STRIK-shun) Decreased diameter of blood vessels.

vasodilation (VAY-soh-die-LAY-shun) Increased diameter of blood vessels.

vasomotor center (vay-soh-MOH-tor) Area of the lower pons and upper medulla oblongata that continually transmits a low frequency of action potentials through sympathetic neurons to smooth muscle in blood vessels; can cause vasoconstriction and vasodilation.

vasomotor tone Partial constriction of blood vessels in the periphery, which results from relatively constant sympathetic

stimulation.

vasopressin (vay-soh-PRESS-in) [L. *vaso,* blood vessel + *pressum,* to press down] See *antidiuretic hormone.*

vein (VANE) Blood vessel that carries blood toward the heart.

venous return (VEE-nus) Volume of blood returning to the heart.

ventilation (ven-tih-LAY-shun) Movement of air in and out of the lungs.

ventral (VEN-tral) [L. *venter,* belly] In humans, synonymous with *anterior.*

ventral root Motor (efferent) root of a spinal nerve.

ventricle (VEN-trih-kel) [L. *venter,* belly] Cavity; in the brain, one of four cavities filled with cerebrospinal fluid; one of two chambers of the heart that pump blood into arteries; there are a left and a right ventricle.

vernix caseosa (VER-niks kay-see-OH-sah) Epithelial cells and sebaceous matter that cover the skin of the fetus.

vesicle (VES-ih-kull) [L. *vesicula,* blister or bladder] Small, membrane-bound sac containing material to be transportedacross the cell membrane.

vestibular fold (ves-TIB-you-lar) [L., entrance hall] False vocal fold.

vestibule (VES-tih-byul) Small cavity or space at the entrance of a canal; see also *vulva.*

villus (VILL-us), pl. **villi** (VILL-eye) [L., shaggy hair] Projection of the mucous membrane in the small intestine that increases surface area.

visceral (VISS-er-al) [L. *viscus,* the soft parts, internal organs] Relating to the internal organs.

visceral peritoneum (per-ih-toh-NEE-um) [L., organ] Part of the serous membranein the abdominal cavity covering the surface of some abdominal organs.

vitamin (VIE-tah-min) [L. *vita,* life + *amine,* from ammonia] One of a group of organic substances, present in minute amounts in natural foods, that are essential to normal metabolism; insufficient amounts in the diet may cause deficiency diseases.

vitamin D Fat-soluble vitamin produced from a precursor molecule in skin exposed to ultraviolet light; increases calcium and phosphate uptake in the intestine.

vitreous humor (VIT-ree-us) Transparent, jellylike substance that fills the posterior compartment of the eye; helps maintain pressure within the eye and holds the lens and retina in place.

vocal fold (VOH-kal) One of the ligaments that extends from the posterior surface of the thyroid cartilage to the paired cartilages of the larynx; the superior pair are the false vocal folds, and the inferior pair are the true vocal folds.

vulva (VUL-vah) [L., a wrapper or covering, seed covering, womb] External genitalia of the female; the mons pubis, labia majora and minora, the clitoris, the vestibule and its glands, the opening of the urethra, and the opening of the vagina.

white blood cell (WBC) Round, nucleated blood cell involved in immunity; includes neutrophils, basophils, eosinophils, lymphocytes, and monocytes; also called a leukocyte.

X-linked Trait caused by a gene on the X chromosome.

yolk sac (YOKE SACK) Highly vascular endodermal layer surrounding the yolk of an embryo.

zona pellucida (ZOH-nah pe-LOO-si-da) [L. *zone,* girdle + *pellucidus,* passage of light] Extracellular coat surrounding the oocyte; appears translucent.

zygomatic (zie-goh-MAT-ik) [G. *zygon,* yoke] Referring to the zygomatic, or cheek, bone; the zygomatic arch is a bony arch created by the junction of the zygomatic and temporal bones.

zygomaticus muscle (ZY-goh-MAT-ih-kus) Muscle originating on the zygomatic bone and inserting onto the corner of the mouth; involved in smiling.

zygote (ZIE-goht) [G. *zygotos,* yoked] Single-celled, diploid product of fertilization, resulting from the union of a sperm cell and an oocyte.

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